RESEARCH ARTICLE

Microstimulation to the Middle Temporal Area and its Effect on the Generation of Microsaccades

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Abstract

It has been repeatedly shown that neural activity in different brain structures can be correlated with perceptual and cognitive functions using electrical microstimulation. Currently, microstimulation is the only method that can demonstrate causal links between neural activity and specific cognitive functions. This study investigates the effects of microstimulation to the MT area of the visual cortex on the production of microsaccades for several seconds. Microsaccades are a type of fixational eye movement characterized by their quickness and low amplitude. The preliminary findings in this paper suggest that microstimulation to the MT area causes an increase in frequency and peak velocity of microsaccades. However, a more in-depth analysis to establish a correlation between the two was unsuccessful. These results suggest further investigation into the effects of microstimulation on microsaccades – using more sophisticated and reliable data collecting and analyzing techniques – is necessary.

Introduction

Microsaccades are involuntary miniature eye movements that occur during extended visual fixation in animals with *foveal vision*. The amplitude of microsaccades varies from 2 to 120 arcminutes (1, 2). The exact physiological role of microsaccades in vision is still a debated topic. Studies have proposed microsaccades to be the mechanism that counteracts drifting of the eyes (3) and visual fading (4). Furthermore, microsaccades have been associated with an increased visual detection threshold (5, 6). This study explores the effect of microstimulation in the middle temporal (MT) area of the visual cortex on the frequency and peak velocity of microsaccades.

Microstimulation is an effective way to manipulate the activity of a small group of neurons with spatial and temporal precision since neurons communicate electrochemically and the electric current induced by the microstimulation can excite or suppress this activity. It is a powerful tool that allows us to observe the behavioral effects of an increase in the output signal of a group of classified neurons. Therefore, microstimulations are widely used to link neural activity with a particular cognitive function (3).

In this study, microstimulations are applied to the MT area of the visual cortex . This region has been shown to be highly selective for coherent motion and is also linked to the computation of three-dimensional structures (4, 5, 6). It was assumed that microstimulations produce percepts that are similar to the ones generated by natural sensory stimuli, however, Masse and Cook (4) showed that microstimulations in the MT area produced weaker but longer-lasting effects on motion perception in comparison to natural visual stimuli.

The effect of microstimulation on microsaccades has not been previously explored in any great detail. Low-amplitude and brief events such as microsaccades are difficult to detect and characterize. We will use microstimulation to explore the neural systems that control visual fixation and microsaccades. Furthermore, we hope to establish a link between the firing properties of the aforementioned neurons and the production of microsaccades.

Experimental Procedure

Two male monkeys (*Macaca mulatta*) were trained to detect a small pulse of coherent motion in a random dot patch. Eye position data was collected from the monkeys using a video based eye tracking system. For this specific study, we used two non-overlapping random dot patches (RDP). The RDPs would display coherent motion for discrete time periods (minimum 19 ms) at random moments during the experimental trial. The level of coherence of the two RDPs was different. The patch with high coherence had 95% coherence in all of

its coherent motion pulses. In other words, 95% of the dots would move in the same direction for the duration of the coherent motion stimulus. The patch with low coherence had 20 to 80% (mean of 30%) coherence in all of its coherent motion pulses. Furthermore, since neurons in area MT are directionally selective, the coherent motion pulse of a RDP was matched to the preferred direction of the overlapping receptive field. Electrical microstimulation was delivered to the receptive fields (one for each RDP) with two low impedance (250-1000 KΩ at 1KHz) microelectrodes using a constant–current dual phase simulator (Bak Electronics). The microstimulation waveform is synchronized with the motion stimulus waveform of the RDP that has low coherence but with a lag of 50 ms. An individual microstimulation pulse had a width of 200 μs and the pulses would be fired at a frequency of 250 Hz. The current levels used ranged from 3 to 50 μA with a median of 12 μA.

The trial would start when the monkey depressed a lever to signal that it had started fixating on a specified point on a screen. The trial would end if the monkey's eye position deviated more than 1.5 degrees from the fixation point. After the lever was depressed, motion started in two random dot patches close to the fixation point. A pictorial representation of this setup can be viewed in Figure 1. The monkey indicated, by releasing a lever, when motion in either of the two patches became correlated, that is to say the instance that the dots had the same pattern of back and forth motion. The coherent motion pulses would occur at random during the trial in either of the RDPs according to an exponential distribution, the flat hazard function. The time limit to indicate correlation begins at the onset of motion (correlated) and lasts until 200 ms after the end of the coherent motion pulse. Eye positions were recorded every 2 ms. (500 Hz) using the eye tracking system.

The trial would end if the lever was released, if the monkey broke fixation, or if the time limit of 200 ms since the end of the last coherent motion pulse for the trial had elapsed. For this study, only the trials where the monkey was able to indicate within the allowed time period that correlation was occurring were used. Failed trials, such as those when the monkey's response was too slow or the lever was not released, and false alarm trials, when the monkey raised the lever despite the fact that there was no correlate motion in the patches, were disregarded.

The animal's head was stabilized using steel head-posts before the beginning of trials. The monkeys were also implanted with recording chambers (Crist Instrument) and craniotomies were performed so that the microelectrodes can be inserted into area MT of the visual cortex (these procedures need only be performed once). Structural MRI scans (1.5 T) were used to verify chamber location and microelectrode placement in area MT. All animal procedures followed guidelines set forth by McGill University's Animal health Care Committee and Canadian Council on Animal Care.

Data Analysis

Microsaccades are ballistic movements and leave behind small linear sequences in the plot of the trajectory of eye movements. Microsaccades occur roughly at a rate of 2 per second. Furthermore, they typically have an average amplitude of 22.6 arc minutes in monkeys (*Macaca mulatta*) (5). Two different techniques were employed to detect microsaccades and the results obtained were identical.

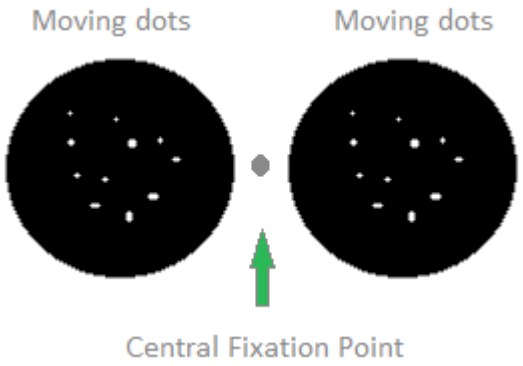

Fig. 1
A schematic of the experimental task that the monkey is trained to perform. The monkey releases a lever when the motion of the moving dots in the two patches becomes correlated.

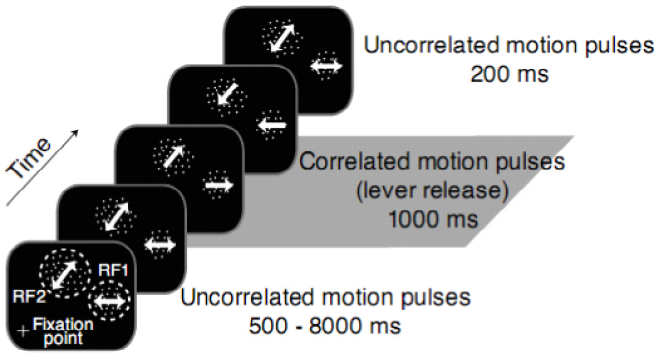

Fig.2
A schematic of the experimental task that the monkey is trained to perform. The monkey releases a lever when the motion of the moving dots in the two patches becomes correlated.

The first method is a modified version of the algorithm described by Engbert and Kliegl (2003). To detect microsaccades in two dimensional velocity space, it first transforms the time series of eye positions into velocities

$$\vec{v_n} = \frac{\vec{x}_{n+2} + \vec{x}_{n+1} - \vec{x}_{n-1} - \vec{x}_{n-2}}{6\Delta t} \qquad (1)$$

where Δt is the time delay between eye position samples, which, in the case of our experiment, would be 2 ms. Equation *(1)* represents a vector of average velocities over 4 position data points. Due to the random orientations of velocity vectors during fixation, the subsequent mean value is zero. As a result of their nature as outliers in velocity space, microsaccades can be detected by tracking their velocities.

The algorithm therefore uses the standard deviation of the velocity distribution as the mechanism for detection. Furthermore, in order to minimize the effect of background noise in the final computation, a median estimator was applied to the time series

$$\sigma_{x,y} = \langle v_{x,y}^2 \rangle - \langle v_{x,y} \rangle^2 \qquad (2)$$

where ⟨⟩ represents the median separator. The detection thresholds for the horizontal ηx and vertical ηy components are computed separately. Additionally, all trials are also computed independently as different trials may have different levels of noise

$$\eta_{x,y} = \lambda \sigma_{x,y} \qquad (3)$$

where λ is the threshold multiplier. To give the best results (see: Engbert and Kliegl (2003)), we use a value of λ= 6 .

The second technique entailed setting a series of parameters that had to be satisfied in order for an eye movement to be defined as a microsaccade. The parameters were obtained from a study on microsaccades by Martinez-Conde *et al.* (2004)(12) and slightly adjusted to compliment the experimental method used to capture eye positions (5). To be deemed a microsaccade, the eye movement had to be between 10 and 300 ms in duration, must start 20 ms after the previous microsaccade, must have a minimum length of 0.05 degrees, and must have no change in eye direction which exceeded 30 degrees for each 5 ms cut of the total time period of the microsaccade.

The accuracy of the two techniques was confirmed by visual inspection of the eye movements and enhanced by the fact that both methods provided identical results.

Results

The purpose of this investigation was to observe the effect of microstimulations on the production and characteristics of microsaccades. In order to conduct this scientific inquiry, we compared trials where there was no microstimulation with trials where microstimulation was introduced in synchrony with the low coherence motion stimulus during the motion detection experiment. An example trial with microstimulation is depicted in Figure 2. The microstimulation waveform is identical to the waveform of the motion stimulus in RDP1 (low coherence) but with a 50 ms delay.

Twenty experimental sessions containing roughly 1000 trials each were analyzed for this study. The conditions for a particular session were constant. Approximately half the trials in each session were experimental, during which we applied microstimulation to the MT of the monkeys. The other half of the trials were control trials. We measured three characteristics of microsaccades: frequency, average peak velocity, and average amplitude. For each session, the three features were computed separately for microstimulation and non-microstimulation trials. Figure 4 is a graphical illustration of the frequency comparison of the twenty sessions.

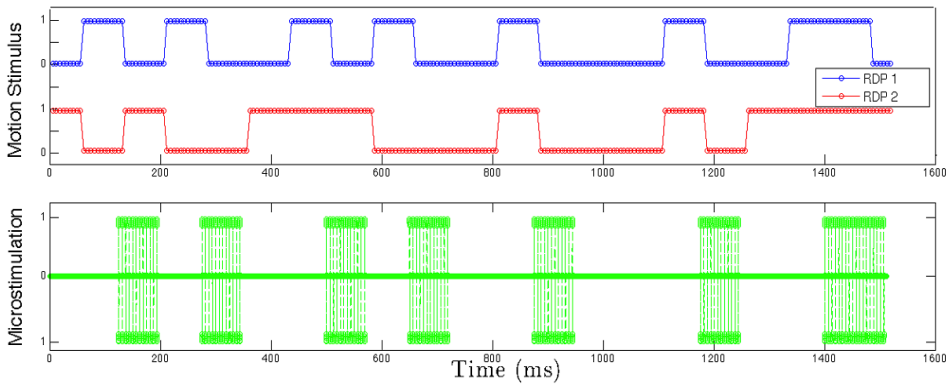

Fig. 3
Top: The motion stimuli of the two RDPs. The motion stimulus in RDP1 (blue) has low coherence (30%) at a value of 1 and no coherence (0%) at a value of 0. The motion stimulus in RDP2 (red) has high coherence (95%) at a value of 1 and no coherence (0%) at a value of 0.
Bottom: The microstimulation waveform. The waveform is in synchrony with the low coherence motion stimulus in RDP1 but with a systematic delay of 50 ms. Neurons in the receptive field overlapping RDP1 are being microstimulated when the value is 1 and there is no current being delivered when the value is 0.

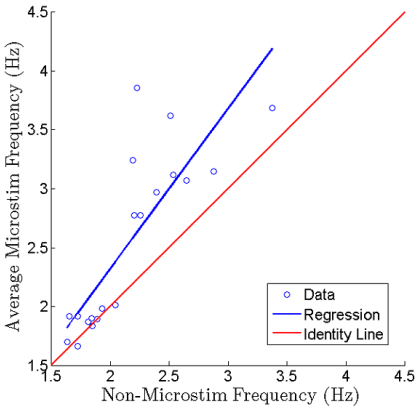

Fig. 4
The vertical axis represents the average microsaccade frequency for all trials across a session with microstimulation. The horizontal axis is the average frequency of the trials with no microstimulation for a particular session. There are twenty data points corresponding to the twenty sessions. The line of best fit has a slope of 1.326, which does not fall within the 95% confidence interval of a slope of one (the identity line), in red.

The figure's vertical axis is the average frequency of the microstimulation trials and the horizontal axis is the average frequency of the trials with no microstimulation. Each data point corresponds to one of the 20 sessions. The line of best fit, derived using a linear regression model, has a slope of 1.3626. It does not fall within the 95% confidence interval of a slope of one (the identity line). The steeper slope indicates that the microsaccade frequency increases for trials where microstimulation is applied to the MT area of the brain.

The average peak velocity across trial types is compared in Figure 5. The difference between average peak velocities of microstimulation and non-microstimulation trials is less prominent than the frequency difference. However, the line of best fit, with a steeper slope of 1.2933, fails to fall within the 95% confidence interval of the identity line. This result implies that the average peak velocity increases when area MT is microstimulated.

The difference in average amplitude was not significant as the line of best fell within the 95% confidence interval of a slope of one. Therefore, it points to no difference in amplitude upon the introduction of microstimulation.

In order to complete the analysis, and to demonstrate that the onset of microstimulation to the MT area was the cause of increase in microsaccade production, we performed a saccade-triggered average (STA) of the low coherence motion stimulus waveforms. The STA computed the average stimulus preceding a microsaccade for 500 ms. The motion stimulus was reduced to scalar values of 1 for coherent motion (low coherence) and 0 for no coherent motion. A comparison of trials with microstimulation and without microstimulation was conducted. Trials with microstimulation, had a corresponding microstimulation pulse for every coherent motion pulse (of the low coherence RDP) after a lag of 50 ms. This synchrony between the two waveforms allowed us to use STA to try to temporally link microstimulation to the generation of microsaccades. The results of the STA are illustrated graphically in Figure 5. It is evident upon inspection that the STA fails to conclusively reveal any correlation between microstimulation and the onset of microsaccades because the difference between the average stimulus for microstimulation and non microstimulation is not strong enough to be satisfactorily distinguished from noise.

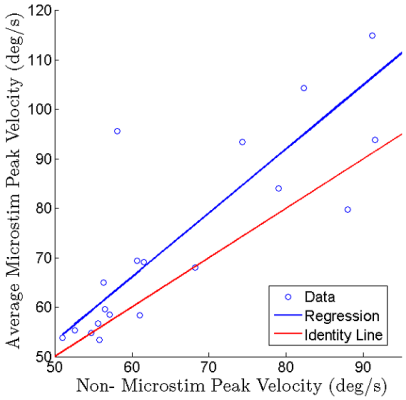

Fig. 5
The vertical axis represents the average peak velocity for all trials across a session with microstimulation. The horizontal axis is the average peak velocity for trials with no microstimulation for a particular session. There are twenty data points corresponding to the twenty sessions. The regression line has a slope of 1.2933 and this value is not within the 95% confidence level of the slope of the identity line (red).

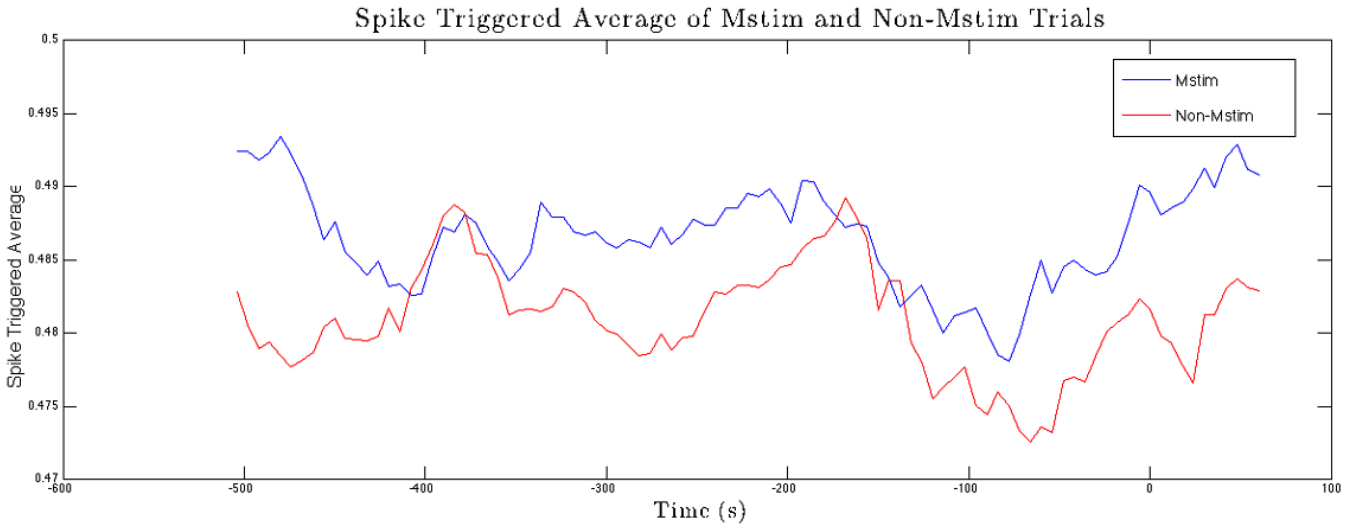

Fig. 6

Saccade-triggered average for trials with microstimulation and without microstimulation. The plot depicts the average motion stimulus 500 ms before the onset of a microsaccade. The motion stimulus used in the STA was from the RDP with low coherence and the stimulus was reduced to two scalar values for computing the average. A value of 1 was assigned when there was coherent motion and a value of 0 was assigned when there was no coherent motion.

Discussion

The initial analysis suggested that microstimulation caused an increase in microsaccade frequency and average peak velocity. Figures 3 and 4 revealed increases in microsaccade frequency and average peak velocity within the microstimulation trials of a session. The frequency appeared to be more affected than the average peak velocity, possibly due to the fact that microsaccades have a very specific velocity range (discussed in Data Analysis). This signifies that they cannot undergo radical velocity change, otherwise they would not be deemed a microsaccade. The STA analysis mentioned in the results section computed the average motion stimulus (from the low coherence RDP) amplitude preceding every microsaccade. This method was carried out in order to locate the burst of microstimulations that caused the extra microsaccdes in microstimulation trials. This was possible since the microstimulation pulses occurred almost concurrently (50 ms delay) with the coherent motion pulses (which were used in the STA analysis) in trials with microstimulation. If microstimulation had caused the increased generation of microsaccades in microstimulation trials, then within a certain time period preceding the microsaccade, we should find a coherent motion pulse, and therefore a corresponding microstimulation pulse. Since the coherent motion pulse has a scalar value of 1, this will cause a peak at some point in time preceding a microsaccade in the STA trace for microstimulation trials. This peak was not found from our STA analysis; as can be observed in Figure 6, there is no significant difference in amplitudes for microstimulation and non-microstimulation trials.

The disparate results of the two analyses creates an ambiguity surrounding the cause of the increase in microsaccade frequency. We were unable to satisfactorily establish any correlation between microstimulation and microsaccades; other explanations must therefore be entertained. The enigma surrounding the results of this study may be explained by the difficulty and unpredictability inherent in delivering microstimulation to MT neurons. For example, the tip position of the electrode can easily be repositioned between trials of the same session; this is due to pulsation of the brain and the moistness of its texture. Also, the two monkeys may have been reacting to the auditory stimuli generated by the onset of microstimulation, since microsaccade generation has known oculomotor mechanisms (7). In order to conclusively determine the effect of microstimulation on microsaccades, further analytical techniques need to be applied to do an exhaustive search for a temporal link between microstimulation and the generation of microsaccades.

Conclusions

The effects of microstimulation to the MT area on the generation of microsaccades were studied. Our preliminary results suggest that microstimulation caused microsaccades to occur more frequently and with a higher velocity. However, a deeper analysis revealed no correlation between the two. Although inconclusive, the results in this paper make this a rewarding avenue for future vision research, with implications for other microstimulation centered studies.

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References

[1] Darwin, R. W.; Darwin, E. "New Experiments on the Ocular Spectra of Light and Colours". Philosophical Transactions of the Royal Society of London 76, 313-348 (1786).

[2] Martin Rolphs. "Microsaccades: Small steps on a long way". Vision Research 49, 2415–2441 (2009).

[3] T.N. Cornsweet. "Determination of the stimuli for involuntary drifts and saccadic eye movements." Journal of the Optical Society of America, 46 pp. 987–993 (1956).

[4] S Martinez-Conde, SL Macknik, XG Troncoso, TA Dyar. "Microsaccades counteract visual fading during fixation". Neuron 49 (2), pp. 297-305 (2006).

[5] Bridgeman B, Palca J. "The role of microsaccades in high acuity observational tasks". Vision Res 20:813-817 (1980).

[6] Rucci M., Iovin R., Poletti M., Santini F. "Miniature eye movements enhance fine spatial detail". Nature, 447 (7146), 851–854 (2007).

[7] Cohen and Newsome. "What electrical micros- timulation has revealed about the neural basis of cognition". Current Opinion in Neurobiology 14, 169–177 (2004).

[8] Masse and Cook. "Behavioral Time Course of Microstimulation in Cortical Area MT". Journal of Neurophysiology 103, 334–345, (2010).

[9] Harrington et al. "The Effect of Microsaccades on the Correlation between Neural Activity and Behavior in Middle Temporal, Ventral Intrapari- etal, and Lateral Intraparietal Areas". The Journal of Neuroscience 29 (18), 5793–5805 (2009).

[10] Bradley, D.C., Chang, G.C., and Andersen, R.A. "Encoding of three-dimensional structure-from-motion by primate area MT neurons." Nature 392: 714-717 (1998).

[11] Engbert, R, Kliegl, R. (2003). "Microsaccades uncover the orientation of covert attention.Vision Research." 43, 1035-1045 (2003).

[12] Martinez-Conde et al. "Microsaccades: A neurophysiological analysis". Trends in Neuroscience 32 (9), pp 463-475 (2009).