SHORT REPORT

Pallidal activity during dystonia: somatosensory reorganisation and changes with severity

F A Lenz, J I Suarez, L Verhagen Metman, S G Reich, B I Karp, M Hallett, L H Rowland, P M Dougherty

Abstract
A woman with progressive, medically intractable right upper limb dystonia underwent a pallidotomy with only transient improvement. During the procedure her dystonia became more severe as she repeatedly made a fist to command in order to provoke dystonia transiently (movement provoked dystonia). Comparisons within cells in the internal segment of the globus pallidus (Gpi) disclosed that the firing rate was the same at rest, with making a fist, and during movement provoked dystonia. However, the firing rate compared between cells decreased significantly throughout the procedure as the patient made a fist repeatedly. During the second half of the procedure the firing rate of cells in the Gpi was similar to that in hemiballismus. The proportion of cells in the Gpi which responded to sensory stimulation was significantly higher in dystonia (53%) than in hemiballismus (13%). These results suggest that pallidal activity can correlate inversely with the severity of dystonia, perhaps due to activity dependent changes in neuronal function resulting from repeated voluntary movement.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Case report and methods
A 45 year old right handed woman presented with slowness of right arm movement progressing dystonia during a pallidotomy, as the second half of the procedure the firing rate decreased throughout the procedure as the patient made a fist repeatedly. During the second half of the procedure the firing rate of cells in the Gpi was similar to that in hemiballismus. The proportion of cells in the Gpi which responded to sensory stimulation was significantly higher in dystonia (53%) than in hemiballismus (13%). These results suggest that pallidal activity can correlate inversely with the severity of dystonia, perhaps due to activity dependent changes in neuronal function resulting from repeated voluntary movement.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Case report and methods
A 45 year old right handed woman presented with slowness of right arm movement progressing dystonia during a pallidotomy, as the second half of the procedure the firing rate decreased throughout the procedure as the patient made a fist repeatedly. During the second half of the procedure the firing rate of cells in the Gpi was similar to that in hemiballismus. The proportion of cells in the Gpi which responded to sensory stimulation was significantly higher in dystonia (53%) than in hemiballismus (13%). These results suggest that pallidal activity can correlate inversely with the severity of dystonia, perhaps due to activity dependent changes in neuronal function resulting from repeated voluntary movement.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity

Dystonia is a movement disorder characterised by sustained muscle contractions leading to twisting movements and abnormal postures. The neuronal mechanism of dystonia is unknown but has been hypothesised to fit the hyperkinetic model of movement disorders. Pallidotomy is reported to be an effective treatment for dystonia and offers the opportunity to study neuronal activity in the disease. We report a patient in which a progressive decrease in firing rates in the internal segment of the globus pallidus (Gpi) correlated with worsening dystonia during a pallidotomy, as the patient made repetitive voluntary movements.

Keywords: globus pallidus; Parkinson’s disease; apomorphine; dystonia; plasticity
Pallidotomy was performed under local anaesthetic block. The locations of the optic tract, internal capsule, cellular, and acellular regions were determined and compared with atlas maps to establish the location of the Gpi. Responses to sensory stimuli were sought for all cells in the GPi and GPe during passive movements of upper and lower limbs, both ipsilateral and contralateral to the recording site. Lesions were made within the part of the GPi where cells responded to passive movements of the limbs.

Postoperatively, neuronal activity was studied for all isolated cells that could be recorded for 120 s including intervals with the arm at rest, during making a fist, and after the arm had achieved the final dystonic posture. The action potentials of single neurons were discriminated and digitised at 10 kHz by a standard shape fitting package (Explorer, Brainwave, Thornton, Colorado, USA) and times of occurrence of action potentials were stored at a clock rate of 10 000 Hz. All quantitative results are firing rates of isolated single neurons calculated as number of action potentials divided by sampling epoch, reported as the median and range and analysed by non-parametric statistical methods (Kruskal-Wallis ANOVA, Statistica, Statsoft, Oklahoma City, OK, USA).

**Results**

The figure illustrates that GPi firing rates in the patient with dystonia at rest (40.8/s, range 20.1–53.6, n=16) were significantly different from Parkinson’s “off” (91/s, range 84.5–103.8, n=21) but were not significantly different from hemiballismus (30/s, range 18.6–41.0, n=13, p>0.05) or Parkinson’s “on” (44.3/s, range 33.9–64.3, n=17, p>0.05). The low frequency modulation and pauses in the firing patterns of cells in the GPi of the patients with Parkinson’s disease, dystonia, and hemiballismus. Spike trains for Parkinson’s disease and average firing rates for all cells are shown for cells studied “off” (uppermost trace), and for those studied “on” (second trace from the top). For the patient with dystonia the spike trains for each cell is shown at rest (labelled rest), as the patient starts to make a fist (onset as indicated by triangle), during maintenance of a fist as the arm moves to final dystonic posture (tonic) and during the final dystonic posture (posture). Two cells are shown which were recorded at different times during the procedure. Time of the cellular recording and firing rates with the patient at rest are indicated for each cell. There is a questionable phasic response to making a fist (triangle) for the cell recorded at 122 minutes after the start of the procedure (dystonia: upper panel). None of the cells recorded showed an obvious response during making a fist.
spike train seemed to be less pronounced in the patient with dystonia than in the patient with hemiballismus but more common than in patients with Parkinson’s disease, either “on” or “off”.

Throughout the exploration of the basal ganglia (245 minutes) the patient with dystonia repeatedly (n=39) made a fist for 1–2 minutes in response to command. As illustrated in the figure, firing rates were not significantly (Kruskal-Wallis ANOVA) different between rest (45.9/s, range 20.1–53.6), making a fist (33.7/s, range 19.6–51.5), and the final dystonic posture (40.7/s, range 17.7–48.3). The dystonia became worse throughout the procedure as indicated by the surgeon’s observation, the patient’s self report, and the significant (r=-0.89, n=37, p<0.001) decrease in the time between making a fist and achieving the final dystonic posture (fist to posture interval).

The firing rates in the Gpi decreased significantly as a function of time during the procedure in the patient with dystonia (r=-0.66, n=16, p<0.01) and as a function of the number of times a fist was made (r=-0.68, n=42, p<0.01). No significant change was seen in either Gpi activity or clinical state during the procedures in any of the six patients with Parkinson’s disease in whom such analysis was performed. The fist to posture interval was directly related (r=0.50, n=16, p<0.05) to the firing rate in the Gpi. During the second half of the procedure in the patient with dystonia (time after beginning of procedure>180 min), firing rates in Gpi (16.9/s, range 12–22) were similar to those in the patient with hemiballismus (30/s, 18.6–40.8).

Firing rates in the GPe were lower in the patient with dystonia at rest (45.9/s, range 27.9–65.3, n=15, Kruskal-Wallis ANOVA, p=0.25) and in hemiballismus (18.1/s, range 7.5–26.5, n=12, p<0.001) than during Parkinson’s “off” (53.4, range 44–80, n=17) or “on” (72.2, range 41.2–105.1, n=9). Firing rates in the GPe were not significantly different (Kruskal-Wallis ANOVA) between rest (45.9/s, range 27.1–65.3), making a fist (48.2/s, range 30–65.3), and the final dystonic posture (44.9/s, range 24.1–61.7). Firing rates in the GPe were not significantly related to fist to posture interval (r=0.31, m=15.8, p<0.25, n=16). Therefore, Gpi firing rates in dystonia decreased progressively throughout the procedure while those in Gpe were tonically less than in Parkinson’s disease.

A higher proportion of cells in Gpi of the patient with dystonia responded to somatosensory stimulation (53%, 9/17), than in hemiballismus (13%, 2/15, p<0.05 Fisher’s exact test), Parkinson’s “off” (23/67, 34%, p<0.05) and Parkinson’s “on” (6/19, 32%, p>0.05). The proportion of Gpi sensory cells was constant in the first (5/9) and second half (4/8) of the procedure in the patient with dystonia. In the two trajectories (one parasagittal plane) through Gpi cells responding to sensory inputs consistently had RFs including the dystonic upper limb (RFs on wrist or hand 5/17 cells). Similar consistency of RFs was never found in a single parasagittal plane of 40 patients with Parkinson’s disease.

**Discussion**

The baseline firing rates of cells in the Gpi decreased into the range found in hemiballismus as the patient with dystonia made repetitive voluntary movements and the dystonia increased in severity. Clinically, the increase in dystonia with voluntary movement is so characteristic that the standard scale for dystonia rates both the disability from dystonia and the degree to which it is provoked by movement. The firing rates compared within cells in the Gpi were not significantly altered from resting levels during either making a fist or movement provoked dystonia. These results suggest that inputs to Gpi in dystonia may undergo activity dependent changes in relation to voluntary movement. During the second half of the procedure firing rates in Gpi are less than in Parkinson’s disease ‘on’ or ‘off’, suggesting that as dystonia becomes more severe neuronal activity changes to fit the hyperkinetic model.

The number of cells with receptive fields was significantly higher (53%) in dystonia than in hemiballismus (13%). Furthermore, all cells with sensory inputs in the patient with dystonia had receptive fields including the dystonic limb which indicates an enlarged sensory representation of the dystonic limb, similar to that found in the thalamus of patients with dystonia. Lesions of the Gpi do not uniformly relieve dystonia, even after the Gpi has reorganised its sensory map, as in the present case (Lozano AM, personal communication, Vitek JL, personal communication, and see Jankovic et al, Vitek et al, and Vitek and Lenz). Therefore, sensory changes in the pallidum alone do not explain dystonia. However, they may distinguish dystonia from hemiballismus, as features of both are consistent with the hyperkinetic model.

In a preliminary report of activity in the basal ganglia during dystonia firing rates of cells in the Gpi were found (48/s) to be similar to those seen in the patient and intermediate between those in hemiballismus and normal monkeys. Activity dependent changes in cellular firing were not noted. Decreased firing rates in the Gpi could explain the disinhibition of cortex in focal dystonia as a result of decreased γ-aminobutyric acid inhibition from the Gpi to the pallidal relay nuclei of the thalamus. The presence of dystonia with “normal” firing rates early in the procedure plus the failure of the lesion to relieve dystonia suggest that altered baseline firing rates are not the primary driver of dystonia in this case.

The inverse relation between dystonia and firing in the Gpi cannot be due to activity dependent changes occurring in the pallidum as within cells analysis disclosed that movements did not alter the firing of pallidal cells. Furthermore, altered activity in the Gpi is not explained by the indirect pathway as decreased firing rates seen in the GPe would be predicted to increase firing rates in the Gpi via the indirect pathway. If the indirect pathway is excluded then the inverse relation may result...
from increased activity in the direct pathway from the putamen to the Gpi. The excitatory corticostriatal connection terminates on N-methyl-D-aspartate, (an excitatory amino acid neurotransmitter) receptors which have the potential to explain activity dependent changes in striatal activity.\textsuperscript{1}\textsuperscript{19–21} On this basis we hypothesise that the inverse relation between Gpi cellular firing and dystonia is the result of activity dependent changes in striatal activity transmitted to the Gpi through the direct pathway.

This study was supported by NIH P01 NS32386-Project 1. We thank Ross Cutler for writing the programs used in this study.

19 Carlson M, Carlson A. Interactions between glutamnergic and monoaminergic systems within the basal ganglia. JNFS 1990; 14:272–6.