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Probabilistic Modeling of Selective Stimulation of the Human Sciatic Nerve with a Flat Interface Nerve Electrode

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Abstract

Proper ankle control is critical to both standing balance and efficient walking. This study hypothesized that a Flat Interface Nerve Electrode (FINE) placed around the sciatic nerve with a fixed number of contacts at predetermined locations and without *a priori* knowledge of the nerve's underlying neuroanatomy can selectively control each ankle motion. Models of the human sciatic nerve surrounded by a FINE of varying size were created and used to calculate the probability of selective activation of axons within any arbitrarily designated group of fascicles. Simulations suggest that currently available implantable technology cannot selectively recruit each target plantar flexor individually but can restore plantar flexion or dorsiflexion from a site on the sciatic nerve without spillover to antagonists. Successful activation of individual ankle muscles in 90% of the population can be achieved by utilizing bipolar stimulation and/or by increasing the number of contacts within the cuff.

I. Introduction

An estimated 5.5 to 6.0 million Americans have a history of stroke and 250 to 450 thousand Americans live with a spinal cord injury (SCI) [1, 2]. Lack of motor control due to these conditions ranges in degree from minor to complete paralysis. A common problem within these populations is foot-drop: a condition in which an individual is unable to partially or fully dorsiflex the foot. Those with foot-drop frequently drag the foot during swing phases of gait and compensate by raising the ipsilateral hip or circumducting the affected leg. These populations also can have diminished or absent plantar flexion, which reduces propulsive force during gait [3]. Both of these deficits could be corrected by stimulating the appropriate axons within the sciatic nerve (SN).

In cat studies, selective and graded muscle contractions have been reported with spiral nerve cuff electrodes placed around [4–9] or a penetrating electrode array placed within the SN [10–14]. Other animal experiments have shown that the Flat Interface Nerve Electrode (FINE) can selectively restore individual functions controlled by the SN [15, 16]. However, the morphology of nerves obtained from animal models differs markedly from that of

humans. For example, the cat SN contains 5 to 10 fascicles whereas the human SN contains 25 to 70, depending on the location along the nerve [17, 18].

With respect to the human SN, selective stimulation is important because various phases of gait require specific ankle motions – dorsiflexion (DF) or plantar flexion (PF) –without the accompaniment of excessive foot inversion (FI) or eversion (FE) or toe flexion (TF) or extension (TE). Proper ankle control is critical to both standing balance and efficient walking. Due to the success of the modeling and intraoperative testing found for electrode design for the human femoral nerve [19], a similar approach was taken to design a neural interface for the human SN. The hypothesis of this study is that a FINE placed around the SN with a fixed number of contacts at predetermined locations and without *a priori* knowledge of the nerve's underlying neuroanatomy can selectively control each ankle motion though individual muscle recruitment.

II. Methods

A. Finite Element Method (FEM) Development

Realistic 3D FEM models of the distal human SN were created from a histological cross section. The nerve contained 27 fascicles. A digitized cross sectional image of the distal SN was imported into MATLAB (Mathworks, Natick, MA). Borders of the epineurium and endoneurium were traced. Traced fascicles were converted into round fascicles while preserving each fascicle's cross sectional area. The perineurium of each fascicle was added at a thickness of 3% of the fascicular diameter [20]. The nerve was reshaped to multiple dimensions to account for varying FINE geometries. Fascicles were assumed to move but not change shape, though this has been demonstrated in animal trials [21]. The coordinates of the neural tissues were used to construct a 3D Finite Element Method (FEM) model in Maxwell 3D V12 (Ansoft, Pittsburgh, PA).

2D neural tissues were extruded to create a 3D semi-infinite model. The tissue properties have been detailed elsewhere [19]. FINES were modeled with opening widths of 10.25, 12.25, and 15.25 mm, opening heights of 2, 2.25, 2.5, 2.75, and 3 mm, and containing 8, 10, 12, 16, 20, 24, or 30 stimulating contacts. Each permutation of opening height and width were modeled except for 2×10.25 mm, which did not contain enough cross sectional area to fit all fascicles without compression. Platinum stimulating surfaces were 0.5×0.5 mm and spaced 1.0 mm on-center [19, 21]. Contacts on the upper inner surface of the cuff were offset from those on the bottom surface, which maximized the space throughout the cuff that could be selectively stimulated.

B. Simulating Axonal Response

Maxwell calculated electrical potentials induced by a 1 mA cathodic current at a single contact. The potentials were exported to MATLAB, where the voltages along axons were interpolated using a 3D cubic spline. Within each fascicle 100 axons with varying diameters were randomly and uniformly distributed from a known distribution [22]. A linear approximation [23] to the MRG double cable axon model [24, 25] was used to determine if an axon propagated an action potential in response to the applied electric field for varied pulse durations. Simulations were run at 50 pulse widths from 0.005 to 0.25 ms and 99 pulse amplitudes from 0.10 to 5.0 mA for monopolar stimulation. For bipolar stimulation, both contacts were considered to be independent and could operate at any of 20 pulse widths and 20 pulse amplitudes within the same ranges.

C. Probabilistic Population Response

Results from the axonal simulations were analyzed to determine which contacts produced the greatest selectivity. Selectivity was defined as the percentage of axons activated within all fascicles innervating a target while limiting the percentage of activated axons not innervating the target to no more than 10% [26, 27]. Unlike the femoral modeling study, information mapping specific fascicles to their respective muscles was not available for the sciatic cross section necessitating adoption of a probabilistic, Monte Carlo inspired approach.

Fascicles within the nerve model were clustered into “groups.” Each group represented a possible target: one or more muscles contributing to a specific function. The number of possible target groups was varied from 9 to 15, representing ideal and non-ideal scenarios, respectively, was based on distal innervation patterns, and was a reduction from the 25 muscles innervated by the distal SN. For each model, 100 unique grouping iterations were created. The percentage of groups in which a required minimum selectivity was obtained was then determined and reported as a probability.

To determine the minimum selectivity required to restore a lost function, an OpenSim [28] biomechanical model of the lower limb was used to assess the magnitude of moments generated by each of 12 muscles innervated by the SN: soleus (Sol), medial and lateral gastrocnemius (MG, LG), tibialis posterior (TP), tibialis anterior (TA), peroneus longus (PL), peroneus brevis (PB), peroneus tertius (PT), flexor hallucis longus (FHL), extensor hallucis longus (EHL), flexor digitorum longus (FDL), and extensor digitorum longus (EDL). These moments were reduced by 50% to account for disuse atrophy [29]. Based on able-bodied moments about the ankle acquired during walking [30], the percentage of the reduced-strength maximum moment required to restore PF or DF during gait was determined. Knowing the relative muscle activation required, the percent of axons innervating the muscle that had to be stimulated was calculated based on the non-linear relationship described by [31]. The percentage of axons that needed to be activated was estimated to be 38%, 40%, 37%, and 14% for the Sol, MG, LG, and PL, respectively. The percentage of axons that needed to be activated for the TA and PB was estimated to be 24% and 11%, respectively. This was under the condition that no spillover to antagonistic muscles occurred. When up to 10% spillover was allowed, these values increased to as high as 57% axonal activation, which was rounded up to 60% to be conservative. To be even more conservative, 90% of the fascicular clusters were required to have axonal activations that achieved the minimum required selectivity.

III. Results

The probability that 60% of the axons within any given cluster of fascicles was activated is shown (Fig. 1). Simulations suggested that at least 16 contacts operated in a bipolar mode were required to achieve the 60% activation level in at least 90% of the population when the nerve contained nine distinct groups of fascicles that needed to be selectively activated. This increased to at least 24 contacts when the nerve contained 10–11 groups of fascicles and to 30 contacts when 12–13 clusters of fascicles needed to be selectively stimulated.

Bipolar stimulation produced greater selectivity than monopolar stimulation and, therefore, increased the probability that 60% of the axons within a fascicular group would be activated. Across all group sizes, the greatest increase in selectivity when using bipolar stimulation was attained for the 16-contact FINE, for which the probability that 60% of the axons within a target fascicular group was activated increased by $42 \pm 4\%$. The increased probability was less for cuffs with fewer or more contacts. Cuff dimensions and the number of fascicular

groups within the nerve had a smaller effect on the increase in selectivity when using bipolar stimulation.

IV. Discussion

The probability of a successful outcome was greatest when bipolar stimulation was used. In fact, bipolar stimulation with an 8-contact FINE was comparable to monopolar stimulation with 20 to 30 contacts. Similar to the results found in [19], for a given cuff dimension, a FINE with more contacts was more likely than a cuff with fewer contacts to selectively recruit a sufficient percentage of axons in any given fascicular group. For a given number of contacts, FINEs with smaller opening heights or widths were more likely to selectively recruit axons as long as the cuff is not too small as to occlude blood flow nor too large to allow for current shunting around the nerve.

The requirement that 60% of the axons were activated in any fascicular group was conservative. If spillover to antagonists can be minimized, the percentage of axons that need to be selectively stimulated is estimated to approach 40% to restore PF and 30% to restore DF. Simulations suggested that the probability of selectively recruiting 40% of the axons within any given fascicular group with a bipolar 8-contact FINE is 80%, which may be acceptable.

Currently available implantable stimulators and FINEs are limited to 16 monopolar and 8 channels, respectively. Under these limitations, simulations suggest that there is a 50% probability of activating at least 40% of the axons within any given fascicular group. Therefore, selective recruitment to the conservative 60% level is unlikely with an 8-contact FINE operated with monopolar stimulation if PF needs to be isolated from DF, FI, FE, TF, and TE. However, activating 40% of the axons in a fascicular group corresponds to approximately 85% of the total muscle force that can be generated. This would translate to approximately 95% of the PF needed during the propulsive phases of gait and would be sufficient to produce the DF force needed during swing-through to prevent foot-drop.

The combination of the required 60% activation level, the 90% successful outcome probability, and the 50% reduction in muscle strength likely makes the overall interpretation of the results too conservative. To satisfy the 90% probability requirement, an 8-contact monopolar FINE is not expected to selectively activate more than 10% of the axons in any fascicular group if there more than 8 fascicular groups within the nerve. However, this cuff satisfied the 90% probability requirement and recruited at least 20% of the axons in any fascicular group when there were only 5 fascicular groups. The ability to isolate 5 distinct groups of fascicles would be sufficient to restore at least 65% of the required moment for PF and 90% of that required for DF but may result in simultaneous recruitment of FI, FE, TF, or TE. Five fascicular groups corresponds to a scenario when there was a group of fascicles responsible for PF and a group responsible for DF surrounded by undesired groups.

Sol, MG, LG, and PL were needed to restore normal PF moments after accounting for disuse atrophy. Similarly, TA and PB were needed to restore balanced DF. However, currently available implantable stimulators are capable of delivering stimulus to only 1 contact at a time. Thus, it is not possible to simultaneously stimulate the number of required muscles unless they all happen to be recruited by the same contact. Stimulators are capable of delivering stimulus with a 1 ms temporal separation between channels. It is unlikely that the 4 ms separating stimulation of the first and last muscle will result in a significant decrease in joint moment compared to simultaneous stimulation of all four muscles when eliciting tetanic contraction. Therefore, selective activation of individual groups of fascicles in a model containing at least 9 groups was a reasonable representation of the physical system.

A primary assumption made in this study was that larger diameter axons were recruited before smaller diameter axons. Generally this is true, but the diameters of activated axons were not taken into account in order to determine the activation level of a muscle. It was for this reason that the aforementioned conservative approaches were taken. Another primary assumption was that the cross section used to develop the models was representative of the population. If the cross section used has far fewer or far more fascicles than what is observed on average, or if this cross section's distribution of fascicular diameters is skewed from what would be expected, the probabilities may no longer apply to the general population. This is unlikely, however, because the cross section was representative of those collected during an anatomical study [17].

V. Conclusion

While distal stimulation on the tibial and peroneal nerves mitigates the hurdles associated with recruiting antagonists, simulations suggest that available implantable technology can restore PF or DF from a site on the sciatic nerve without spillover to each other, but cannot selectively recruit each target plantar flexor individually nor avoid FI, FE, TF, or TE. Adding more channels or operating in a bipolar mode would allow the FINE to restore all six functions.

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Fig. 1.

The probability of activating at least 60% of the axons within any group of fascicles in the sciatic nerve models. Individual rows correspond to the three FINE widths. Individual columns correspond to the five FINE heights. The right half illustrates the effects of bipolar stimulation. The seven minor sub-columns of both major columns show the effect of varying the number of fascicle groups within the model between 9 and 15. White boxes: no model