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# SELECTIVE STIMULATION OF THE HYPOGLOSSAL NERVE: A FINE APPROACH TO TREATING OBSTRUCTIVE SLEEP APNEA

P. B. Yoo[1], M. Sahin[2] and D. M. Durand[1]
[1]Neural Engineering Center, Dept. of Biomedical Engineering Case Western Reserve University, OH, USA
[2]Dept. of Biomedical Engineering, Louisiana Tech University, LA, USA

*Abstract* – **Isolated activation of the tongue protrusor muscles is the current technique for treating obstructive sleep apnea (OSA) via functional electrical stimulation. Recent studies, however, have shown marked improvements in upper airway (UAW) patency by co-activating the tongue protrudor and retractor muscles. As such, selective stimulation of the hypoglossal (XII) nerve with a single implantable device presents an attractive alternative for treating OSA.**

**In order to demonstrate the feasibility of such a device, the maximum achievable stimulation selectivity of the Flat Interface Nerve Electrode (FINE) was investigated. The beagle XII nerve was stimulated with an implanted FINE, while the corresponding neural and muscular responses were recorded.**

**The overall performance of the FINE, as defined by the selectivity index (SI), showed a high degree of selectivity at both the fascicular and muscular levels: 0.91 ± 0.05 (n = 5) and 0.85 ± 0.03 (n = 4), respectively.**

**The results clearly demonstrate the feasibility of the FINE for selective stimulation of the XII nerve and UAW muscles.**

*Keywords* – **hypoglossal nerve, selective stimulation, obstructive sleep apnea, electroneurogram, electromyogram**

## I. INTRODUCTION

Obstructive sleep apnea (OSA) is commonly characterized by recurrent obstructions of the upper airway (UAW), arterial oxygen desaturation and repeated arousals from sleep. Referred to as the snorer's disease, it is suggested that OSA involves a gradual degeneration in UAW mucosal receptors along with the progressive deposition of lipid tissue in the UAW lumen. It is this narrowing of the UAW that initiates larger negative pressure swings during inspiration and, as a result, predisposes such individuals to OSA.

Methods currently employed to treat OSA range from non-invasive approaches such as Continuous positive applied pressure (CPAP) to more invasive surgical procedures such as Uvulopalatopharyngoplasty (UPPP) and tracheostomy. These modes of treatment, however, have been limited in their compliance and/or applicability.

Electrical stimulation of the Hypoglossal nerve (XII) is an alternative method for treating OSA. Its efficacy has been demonstrated in both experimental and clinical settings. By stimulating the medial branch of the XII (genioglossus muscle), the UAW resistance and number of apneic episodes were reduced in animal models and human patients, respectively [1]. It is not clear, however, that this technique will sustain UAW patency during obstructed inspiration.

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Fuller et al. demonstrated the advantages of co-activating both the protrudor and retractor muscles in rats, via stimulation of isolated XII fascicles. In addition to improved airflow of the UAW, co-activation also significantly decreased pharyngeal collapsibility [2].

The flat-interface-nerve-electrode (FINE) presents a rather unique approach to co-stimulating the functionally disparate branches of the XII. As a result of reshaping the nerve and moving axons closer to the electrode [3], the activation level of each fascicle can be controlled without compromising the perineurium or using large steering currents to localize the excitation.

The objective of this study was to investigate the feasibility of the FINE for OSA treatment, by demonstrating the maximum stimulation selectivity of the electrode. The electroneurogram (ENG) and electromyogram (EMG) signals from the target fascicles and muscles, respectively, were used to compute a selectivity index (SI) that quantified the selectivity of the FINE.

## II. METHODOLOGY

Five adult beagles (9-12 kg) were anesthetized with an initial I.V. injection of Pentothal (1ml/kg) and subsequent ventilation of 1-3% halothane mixed with 100% Oxygen. A schematic of the experimental setup is given in Fig. 1. An incision was made along the midline of the submandibular region to expose and dissect the XII nerve and extrinsic tongue muscles. The branching point of the XII nerve trunk

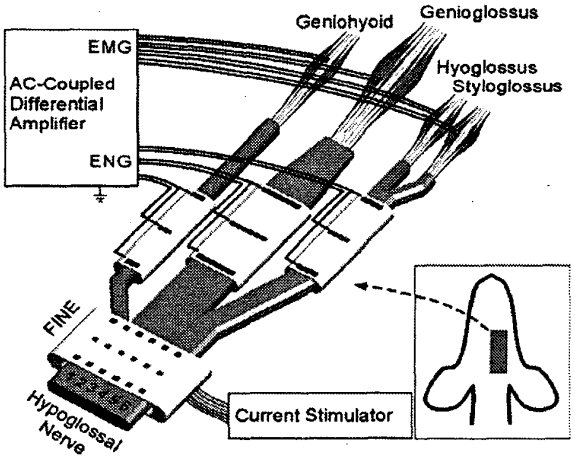


Fig. 1. The site of implantation in the submandibular region of the supine beagle is given in the inset. [Geniohyoid (GH); Genioglossus (GG); Hyoglossus (HG); Styloglossus (SG)]

identified the site for implanting the 12-tripole (i.e. center cathode and adjacent anodes)FINE. Recording FINEs were implanted on the three XII branches and each innervated muscle was implanted with a pair of stainless steel wires (2~5mm separation

As the 12 tripoles of the FINE were sequentially stimulated, the ENG (i.e., compound action potential (CAP)) and EMG were recorded. The current amplitude for each tripole (pulse width = 50 μs; frequency = 2 Hz; number of pulses = 16) was increased from threshold to 1mA.

Using the normalized peak-to-peak voltages ($V_b$), the selectivity was computed from (1), where the target fascicle or muscle determined the assignment of the selectivity as FASCi or FUNCi, respectively. Stimulation was considered selective under the following conditions: a) target $V_b \geq 0.8$ and b) the maximum $V_b$ of each non-target is 0.2. Hence, a FASCi or FUNCi $\geq 0.67$ would specify selectivity.

$$\text{FASCi or FUNCi (ENG or EMG)} = \max\left[\frac{Vb\ (\text{target})}{Vb\ (\text{target + non-target})}\right] \quad (1)$$

The overall performance of the FINE was termed the selectivity index ($0 \leq SI \leq 1$), which is the average selectivity (FASCi or FUNCi) for all respective targets.

Finally, XII nerve innervation was verified as each branch was stimulated while EMG signals were recorded.

## III. Results

Fig. 2 shows consistent co-innervation of branch 3 into the HG and SG. As such, the average $V_b$ of these two functionally similar (i.e., tongue retractor) muscles was used to compute the FUNCi. Branches 1 and 2, however, mainly innervate single muscles: GH and GG, respectively.

An example of recruitment curves are presented in Fig. 3, where the normalized responses were plotted as a function of current. In this case, the stimulating tripole is selective for branch 3 (HG/SG), from threshold to 0.2 mA.

The mean selectivity values (see Table1) for branch 2 (0.76-0.85) indicate a lower selectivity than those for branches 1 and 3. However, the SI confirms an overall high degree of selectivity at both the fascicular and muscular levels: $0.91 \pm 0.05$ and $0.85 \pm 0.03$, respectively.

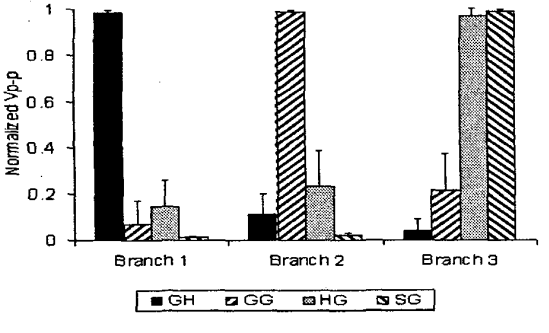


Fig. 2. Fascicle mapping of the XII nerve (n = 4).

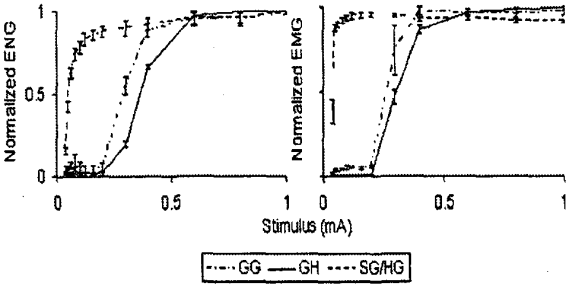


Fig.3. Recruitment curves via stimulation of tripole 6 (refer to Fig.1)

## IV. Discussion and Conclusions

Selectivity can be alternatively understood as a measure of the average non-target activity, for a given level of target activation ($V_b \geq 0.8$). For example, the selectivity for branch 1 (FASCi = 0.95, see Table1) implies that for any implanted FINE, the average non-target activity in (1), will be only 4.2% of its total (i.e., fascicles 2 and 3) activity when stimulating at least 80% of fascicle 1. This is very selective, considering the level of target activation.

The total average non-target activity for branch 2 (FUNCi = 0.76), however, is 25% (GH and HG/SG). This reduced selectivity is mainly attributed to the position of the stimulating tripole and the size of the fascicle. This latter point is supported by finite element models that show a general decrease in selectivity for larger fascicles [4].

Overall, this study demonstrates the feasibility of selectively stimulating the UAW muscles with the FINE.

**TABLE1.**
Mean selectivity for each target nerve/muscle: mean ± SEM.

| | Branch1 (GH) | Branch2 (GG) | Branch3 (HG/SG) |
|---|---|---|---|
| FASCi (n=5) | 0.95±0.05 | 0.85±0.13 | 0.93±0.07 |
| FUNCi (n=4) | 0.85±0.02 | 0.76±0.11 | 0.93±0.04 |


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