




ORIGINAL RESEARCH

Changes in breath cycle sensing affect outcomes in upper airway stimulation in sleep apnea

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Abstract

Background: Upper Airway Stimulation (UAS) is a well-established therapy option for obstructive sleep apnea (OSA).

Aims: There are no data on whether respiratory sensing contributes to successful UAS therapy.

Materials & Methods: After initial measurements of 3 implanted patients (M1), the sensing signal was inverted (M2) without changing other parameters. Two weeks later, the signal was converted back again, and the sensitivity of breathing cycle detection was turned to a very low state (M3).

Results: At M2 and M3, the apnea-hypopnea index and oxygen desaturation index increased.

Discussion: Correct respiratory sensing is important for controlling OSA using UAS.

Conclusions: Therefore, implant centers should optimize respiratory sensing placement and adjustment.

KEYWORDS

breathing cycle, hypoglossal nerve stimulation, PAP failure, PAP intolerance, respiratory sensing, sleep apnea, upper airway stimulation

1 | INTRODUCTION

Hypoglossal nerve stimulation with respiratory sensing (upper airway stimulation [UAS]) has gained increasing interest for the treatment of patients with obstructive sleep apnea (OSA) and positive airway pressure failure. To achieve success rates of about 70%^{1,2} and intensive usage,³ appropriate candidate selection^{4,5} and precise identification of the branches of the hypoglossal nerve are needed.⁶ The electric field—arising from the different modes of electrode configuration in the implant—influences the patient's tongue motion patterns,⁷ which are regarded to be a predictor of response to therapy.⁸

Other elements in the system are a sensing lead and an activation program for the stimulator based on the swings in extrapleural pressure. Previous research has not addressed whether respiratory sensing influences therapy outcomes physiologically. Therefore, the aim of this study was to investigate changes in the quality of control of sleep disordered breathing under UAS treatment as a function of sensing.

2 | REPORT OF CASES

Patients were selected from a University-affiliated Department of Otorhinolaryngology with an experience of over 90 UAS implants. The selection criteria for the initial three patients were as follows: at least 6 months after implantation, therapy responder with an apnea-

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hypopnea index (AHI) below 20/h at the initial study visit (M1), therapy usage stable with at least 4 hours per night, and good sensing signal. We screened our database of UAS patients for potential subjects meeting the inclusion criteria. These patients were then contacted for willingness to participate. The main reasons that patients declined to participate was lack of time or living too remote from the center. There were no incentives given to participants.

This protocol was approved by an ethics committee (AZ 17-344, 15 December 2017).

To evaluate the effects of a change in sensing mode, a type 4 home sleep test (HST) using peripheral arterial tone (WatchPAT, Itamar) was

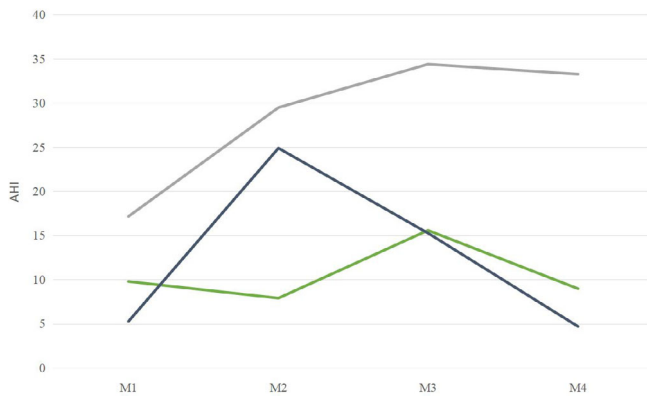


FIGURE 1 Changes in apnea-hypopnea index (AHI) for three patients after initial assessment (M1), with inverting sensing signal (M2), with turning down the sensing signal (M3) and at final assessment (M4). Patient 1: green line; patient 2: blue line; and patient 3: gray line

TABLE 1 Changes in objective and subjective sleep apnea severity, daytime sleepiness assessment, therapy usage, and percentage of supine position during study for all three patients

	Patient number	Preimplantation assessment	Initial assessment	Inverting sensing signal	Turning down sensing signal	Final assessment
AHI in events per hour	1	54.0	9.8	7.9	15.6	9.0
	2	23.5	5.3	24.9	15.3	4.7
	3	27.0	17.2	29.5	34.4	33.3
AHI supine in events per hour	1	NA	10.1	22.3	11.4	10.6
	2	37.0	6.6	24.9	51.1	2.9
	3	32	18.0	42.1	34.4	40.6
ODI in events per hour	1	30.0	2.0	1.4	6.4	2.5
	2	9.5	1.8	10.6	10.6	2.1
	3	11.0	4.9	12.6	12.1	17.1
ESS in points	1	7	4	7	6	5
	2	15	6	6	2	2
	3	17	6	11	4	13
Usage per night in hours	1	NA	6.4	6.4	1.6	6.6
	2	NA	4.5	3.8	2.6	5.9
	3	NA	7.4	1.9	3.3	1.2
Supine position in %	1	NA	93.3	57.8	32.6	37.4
	2	40.1	38.5	38.2	13.1	41.9
	3	74.3	88.1	54.8	82.1	75.3

Abbreviations: AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; ODI, oxygen desaturation index.

used, which lowers inter-rater variability. For a reduction of night-to-night variability, a two-night HST assessment was scheduled.

There were four study time points with an approximate interval of 2 weeks between assessments:

- M1: Initial HST assessment reassuring therapy adherence and effects, including daytime sleepiness using the Epworth Sleepiness Scale (ESS) under therapy.
- M2: Converting the sensing signal from inverse ON to OFF or from OFF to ON. Assessing therapy effects with ESS and a two-night HST assessment.
- M3: Returning the sensing signals to the initial values (M1) and reducing the sensitivity of the breathing cycle detection to a very low state. Assessing therapy effects with ESS and a two-night HST assessment.
- M4: Returning all changes made at M3 the initial values. Assessing therapy effects with ESS and a two-night HST assessment.

Patients were not blinded to the changes in sensor settings.

Statistical analysis and plotting were done using R (Version 3.5.3), an open source environment for statistical computing and graphics, as well as Version 22.0 of the Statistical Package for the Social Sciences software (SPSS, Chicago, Illinois). As the number of subjects in the study was quite low and since data therefore appeared to be skewed and not normally distributed, quantitative data were reported as median (\pm range).

3 | RESULTS

We included all three patients who agreed to participate. As the local ethics committee monitored the first three cases, no additional cases

were allowed, as we already had demonstrated negative effects in all three subjects. Patient 1, with a BMI of 26.0 kg/m² at M1, was implanted 62 months prior to enrolling in this study with a preimplantation AHI of 54/h and oxygen desaturation index (ODI) of 30/h. Patient 2, with a BMI of 30.4 kg/m² at M1, received UAS 40 months prior to this study with a preimplantation AHI of 23.5/h and ODI of 9.5/h. Patient 3, with a BMI of 26.8 kg/m² at M1, was implanted 10 months ago prior study enrollment with a preimplantation AHI of 27/h and ODI of 11/h. All patients were male.

At almost every point in time, a two-night HST assessment was performed. However, for one subject at M2 (inverted sensing signal), there was only one measurement because of a technical failure (patient 3; M1). All respiratory parameters worsened (Figure 1), with the oxygen saturation especially worsening when the sensing lead was turned down (Table 1). Daytime sleepiness was stable over the study period, but usage declined especially with turning down the sensing lead (M3; Figure 1). Regarding the subjective feeling for sensing changes, one patient (patient 3) reported a mixture of no change at all with either condition M2 or M3, whereas two had an awkward feeling during stimulation, especially when inverting the sensing signal (M2).

4 | DISCUSSION

This case series of three patients reports the first structured evaluations of the effect of breathing cycle sensing. Both inverting the respiratory sensing lead and reducing the sensing lead sensitivity worsened the ODI, the AHI, and especially the supine AHI. This suggests that correct respiratory signaling is important for controlling OSA using selective stimulation of the hypoglossal nerve. In an otherwise stable OSA control group receiving UAS (by well-defined interventions at M2 and M3), it was shown that breath sensing and the resulting timed stimulation was disturbed. Therefore, well-adjusted respiratory sensing appears to be necessary for appropriate treatment effects with UAS therapy.

Patient's characteristics with regard to middle age, male gender, and moderate to severe OSA were in correspondence with previous reports in larger cohorts.^{1,2} Therapy usage was high at initial assessment but did not differ from other UAS publications.¹⁻³ In contrast to previous documentation of treatment courses,⁹ time in the supine position changed, especially with regard to the M1 setting. Initially, the AHI for the entire night and in supine position was almost equal. The AHI in supine position increased two to three times more than the AHI for the entire night. Moreover, the ODI worsened at both M2 and M3 for the entire night and in supine position (Table 1).

It could be argued that stimulation at any point in any part of the respiratory cycle could have favorable effects. If the airway was initially open slightly during inspiration, the stimulation would enhance inspiratory dilation. On the other hand, if stimulation occurred during expiration or extended from mid-inspiration to expiration, it would be the time dependence of tissue relaxation that would determine the size of the airway during inspiration without stimulation. However, in our study, these subtle effects could not be detected. In these three

patients, altering respiratory sensing lead stimulation worsened OSA control suggesting that optimization of respiratory sensing is important for optimal disease control. Unfortunately, our sample is limited and does not address longer time intervals or subtle changes in the duty cycle or stress relaxation on the effectiveness of timed stimulation.

Most previous reports on patient reported outcomes document changes in time points with larger intervals.^{1,2} Thus, intervention periods that were too short could be the reasons for the mismatch of unchanged ESS and documented sleep architecture.¹⁰

5 | CONCLUSION

In summary, correct respiratory signaling supports controlling OSA using selective stimulation of the hypoglossal nerve, which has to be respected during implantation and therapy adjustment.

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CONFLICT OF INTEREST

A.S., J.U.S., and C.H. are study investigators, consultants and received honoraria and travel expenses (outside the submitted work) for invited talks on behalf of Inspire Medical, Inc. B.H. and K.H. received travel expenses from Inspire Medical, Inc. K.S. is a site principle investigator of post-FDA studies for Inspire Medical, and a consultant to Sommetrics, 7 Dreamers, and Galvani Bioelectronics. M.V.S. is an investigator for Inspire Medical.

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