

Difficulty Falling Asleep is Associated with Poorer Therapeutic Outcomes in Unilateral Hypoglossal Nerve Stimulation

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Purpose: The coexistence of insomnia and obstructive sleep apnea (OSA) is very prevalent. Hypoglossal nerve stimulation (HGNS) is an established second-line therapy for patients suffering OSA. Studies investigating the effect of the different aspects of insomnia on the therapeutic outcome are largely missing. Therefore, this study aimed to understand the impact of the different aspects of insomnia on the therapeutic outcome under HGNS therapy in clinical routine.

Patients and Methods: This is a retrospective study including 30 consecutive patients aged 55.40 ± 8.83 years (8 female; 22 male) undergoing an HGNS implantation in our tertiary medical center between 2020 and 2023. All patients underwent preoperative polysomnography (PSG) according to AASM. First follow-up PSG was performed 95.40 ± 39.44 days after activation (30 patients) and second follow-up PSG was performed 409.89 ± 122.52 days after activation (18 patients). Among others, the following PSG-related parameters were evaluated: apnea–hypopnea index (n/h) (AHI) and oxygen desaturation index (n/h) (ODI). Insomnia was assessed by the insomnia severity index (ISI) questionnaire. Preoperatively, all patients included filled out each ISI item. Spearman's-rho correlation coefficient was calculated for correlations.

Results: Preoperative score of ISI item 1 (difficulty falling asleep) was 1.93 ± 1.34 and preoperative cumulative ISI score (item1-7) was 18.67 ± 5.32 . Preoperative AHI was 40.61 ± 12.02 (n/h) and preoperative ODI was 38.72 ± 14.28 (n/h). In the second follow-up, the mean difference in AHI was $\Delta 10.47 \pm 15.38$ (n/h) and the mean difference in ODI was $\Delta 8.17 \pm 15.67$ (n/h). Strong significant correlations were observed between ISI item 1 (difficulty falling asleep) and both Δ AHI ($r: -0.65, p=0.004$) and Δ ODI ($r: -0.7; p=0.001$) in the second follow-up.

Conclusion: Difficulty falling asleep may hence negatively influence HGNS therapeutic outcome. Insomnia-related symptoms should be considered in the preoperative patient evaluation for HGNS.

Keywords: hypoglossal nerve stimulation, obstructive sleep apnea, insomnia, polysomnography

Introduction

Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder. OSA is characterized by recurrent episodes of partial and/or complete upper airway obstructions during sleep that lead to apnea and hypopnea.¹ Besides OSA, insomnia is another highly prevalent sleep disorder. Insomnia is defined as an individually reported difficulty with sleep.² Even though both are considered as separate diseases, they often occur concomitantly. Insomnia-related symptoms are reported by up to 50% of patients suffering OSA and up to 40% of patients suffering from chronic insomnia also meet the diagnostic criteria for OSA.³ The coexistence of insomnia and obstructive sleep apnea (COMISA) is clinically highly relevant. COMISA is associated with worse therapeutic outcomes and higher costs compared to the treatment of either OSA or insomnia.^{4,5} The standard in OSA therapy is continuous positive airway pressure (CPAP) therapy.⁶ Hypoglossal nerve stimulation (HGNS) is an established therapeutic option for patients not tolerating PAP-therapy.⁷ PAP-therapy

compliance is especially reduced in patients suffering COMISA.⁸ Previous studies have reported an association between insomnia and poorer apnea–hypopnea index (AHI) reduction⁹ as well as shorter usage of HGNS during the night¹⁰ and patient-reported outcomes such as daytime sleepiness.^{9,11} In contrast, one study showed no significant difference in therapy adherence and efficacy between ISI severity subgroups.¹² Insomnia is a complex sleeping disorder involving different symptoms such as difficulty falling asleep, difficulty staying asleep and/or waking too early, and is often related to hyperalertness and fatigue.¹³ Insomnia may be suspected by a brief screening seven-item questionnaire named the insomnia severity index (ISI) addressing all aforementioned aspects.¹⁴ A few studies already aimed to investigate the impact of insomnia on objective and patient-reported outcomes such as AHI reduction, therapy adherence and daytime sleepiness.^{9–12} However, studies investigating the effect of the different aspects of insomnia on the therapeutic outcome are largely missing. Therefore, this exploratory study aimed to understand the impact of the different aspects of insomnia on the therapeutic outcome under HGNS therapy in clinical routine.

Materials and Methods

This study included 30 consecutive patients undergoing an implantation of inspiration-coupled HGNS (Inspire Medical Systems, Inc., Golden Valley, MN, USA) between 2020 and 2023. Patients included had to fulfil the indication criteria for HGNS therapy¹⁵ such as intolerance to PAP therapy, body mass index (BMI) < 35 kg/m², absence of complete velar concentric collapse on drug-induced sleep endoscopy (DISE), apnea–hypopnea index (AHI) 15–65/h with <25% central apneas on polysomnography (PSG), and the absence of chronic major psychiatric or neurodegenerative disease. All patients included had filled in a complete preoperative ISI questionnaire. The German version of the ISI questionnaire was used.¹⁶ The following questions are included and must be voted on a five-point Likert scale:

Please rate the CURRENT (ie LAST 2 WEEKS) SEVERITY of your insomnia problem(s)

1. Difficulty falling asleep
2. Difficulty staying asleep
3. Problems waking up too early
4. How satisfied/dissatisfied are you with your current sleep pattern?
5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?
6. How worried/distressed are you about your current sleep problem?
7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (eg daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc). currently?

An increasing score indicates an increasing clinically relevant insomnia.¹⁴ All patients underwent preoperative polysomnography (PSG) according to the AASM standard. Furthermore, a velar concentric collapse was ruled out by preoperative DISE. First PSG follow-up was performed 95.40 ± 39.44 days after activation and second follow-up was performed 409.89 ± 122.52 days after activation. First follow-up was performed in all 30 patients, second follow-up was performed in 18 patients. All follow-up PSGs were performed without any in-laboratory titration. Stimulation parameters under PSG were identical to the patient's stimulation parameters as used at the patients' homes for at least one week before in-laboratory PSG.

The following PSG-related parameters were investigated: apnea–hypopnea index (n/h) (AHI), cumulative time under apnea and hypopnea (min), snoring index (n/h) (SI), oxygen desaturation index (n/h) (ODI), percentage of total sleep time under oxygen saturation lower than 90% (t90) and total number of arousal events per hour (arousal index (n/h)). PSG was evaluated by our team's experts in the field of sleep medicine.

All patients provided informed consent to the use of their data for research purposes. The data were evaluated in a pseudonymized fashion. Only health data that are collected in the clinical routine were analyzed retrospectively. So-called “third parties” did not have access to the data and publication occurs exclusively in anonymized form. The Ethics Committee of the Rhineland-Palatinate Medical Association refrains from providing advice in such cases, citing the State Hospital Act (§36 and §37) (see also: <https://www.laek-rlp.de/ausschuesse-kommissionen/ethikkommission/>).

Statistical Analysis

Statistical analysis was performed using SPSS 27 (IBM, Armonk, NY, USA). All data were expressed as mean \pm standard deviation. Wilcoxon's signed-rank test was performed for inner-group comparison. Preoperative as well as for the short-term follow-up all patients included filled out each ISI item. Only 12 patients filled out each ISI item in the long-term follow-up. Spearman's-rho correlation coefficient was calculated for correlations. $p < 0.05$ was considered a statistically significant result. For correlation coefficients Bonferroni correction was performed. Therefore $p < 0.004$ was considered a statistically significant result. Post-hoc power calculation was performed using an online power calculator¹⁷ with $\alpha = 0.05$ and $n = 18$.

Results

Patients were aged $M = 55.40 \pm 8.83$ years at the time of implantation of the HGNS system with an average BMI of $M = 29.69 \pm 4.32$ kg/m². Eight patients were female, 22 patients were male. Preoperative AHI was $M = 40.61 \pm 12.02$ (n/h), preoperative complete time of apnoea and hypopnea was $M = 86.2 \pm 40.2$ (min), preoperative snoring index $M = 244.26 \pm 181.14$ (n/h), preoperative ODI was $M = 38.72 \pm 14.28$ (n/h), preoperative t90 (%) was $M = 8.85 \pm 10.35$ and preoperative arousal index was $M = 23.68 \pm 15.59$ (n/h).

Preoperative scores of the separate ISI questionnaire were as follows: Question 1 was $M = 1.93 \pm 1.34$, question 2 was $M = 2.8 \pm 1.00$, question 3 was $M = 1.97 \pm 1.27$, question 4 was $M = 3.5 \pm 0.73$, question 5 was $M = 2.33 \pm 1.21$, question 6 was $M = 3.20 \pm 1.03$, question 7 was $M = 2.97 \pm 1.13$. Mean of cumulative preoperative ISI was $M = 18.67 \pm 5.32$ (Table 1). Mean of cumulative ISI was $M = 12.7 \pm 6.62$ in the short-term follow-up and $M = 10.08 \pm 7.13$ in the long-term follow-up. Preoperative cumulative ISI and cumulative ISI in the short-term follow-up differed ($p < 0.001$) significantly as well as in the long-term follow-up ($p = 0.003$). Preoperative Cronbach's Alpha for items 1–7 was $\alpha = 0.8$ (Table 1).

In the short-term follow-up, the mean difference in AHI was $\Delta 15.01 \pm 12.15$ (n/h), the mean difference in complete time of apnea and hypopnea was $\Delta 34.40 \pm 36.31$ (min), the mean difference in snoring index was $\Delta 89.68 \pm 115.43$ (n/h), the mean difference in ODI was $\Delta 9.18 \pm 13.21$ (n/h), the mean difference in t90 was $\Delta 2.49 \pm 11.47$ (%) and the mean difference in arousal index was $\Delta 8.38 \pm 16.51$ (n/h) (Table 2).

In the long-term follow-up, the mean difference in AHI was $\Delta 10.47 \pm 15.38$ (n/h), the mean difference in complete time of apnea and hypopnea was $\Delta 25.78 \pm 34.23$ (min), the mean difference in snoring index was $\Delta 65.81 \pm 158.75$ (n/h), the mean difference in ODI was $\Delta 8.17 \pm 15.67$ (n/h), the mean difference in t90 was $\Delta 3.94 \pm 10.44$ (%) and the mean difference in arousal index was $\Delta 1.23 \pm 14.32$ (n/h) (Table 2).

In the short-term follow-up, no significant correlations were shown between the separate score for each one out of the seven ISI items and Δ AHI, Δ cumulative time of apnea and hypopnea, Δ snoring index, Δ ODI, Δ t90 or Δ arousal index (Table 3).

In the long-term follow-up, significant strong negative correlations were shown between question one of the ISI questionnaire and Δ AHI ($r: -0.65$, $p = 0.004$), Δ ODI ($r: -0.7$; $p = 0.001$), Δ t90 ($r: -0.51$; $p = 0.03$) and Δ arousal index ($r: -0.64$; $p = 0.04$) (Table 4 and Figures 1 and 2).

A post-hoc power of 0.87 for the correlation coefficient between question one of the ISI questionnaire and Δ AHI ($r: -0.65$) and a post-hoc power of 0.93 for the correlation coefficient between question one of the ISI questionnaire and Δ ODI ($r: -0.70$) were calculated.

Table 1 ISI Score in the Preoperative, Short-Term Follow-Up and Long-Term Follow-Up

	ISI Score M (SD)	ISI 1 M (SD)	ISI 2 M (SD)	ISI 3 M (SD)	ISI 4 M (SD)	ISI 5 M (SD)	ISI 6 M (SD)	ISI 7 M (SD)	Cronbach's Alpha for Items 1–7
Preoperative	18.67 \pm 5.32	1.93 \pm 1.34	2.80 \pm 1.00	1.97 \pm 1.27	3.50 \pm 0.73	2.33 \pm 1.21	3.20 \pm 1.03	2.97 \pm 1.13	0.80
Short-term	12.70 \pm 6.62	1.47 \pm 1.22	1.97 \pm 1.30	1.37 \pm 1.03	2.13 \pm 1.17	1.73 \pm 1.23	1.93 \pm 1.46	2.17 \pm 1.23	0.88
Long-term	10.08 \pm 7.13	1.17 \pm 1.19	1.75 \pm 0.97	1.42 \pm 1.31	1.67 \pm 1.23	1.25 \pm 1.06	1.00 \pm 1.04	1.50 \pm 1.38	0.91

Notes: Preoperative, short-term and long-term ISI score and score for each item of the ISI; Cronbach's alpha for items 1–7; preoperative ($\alpha = 0.80$), short-term ($\alpha = 0.88$) and long-term ($\alpha = 0.91$).

Table 2 Patients and PSG Parameters

	Preoperative Parameter M (SD)	Δ Short-term Follow-up M (SD)	Δ Long-term Follow-up M (SD)
Age (years)	55.40 ± 8.83		
BMI (kg/m ²)	29.69 ± 4.32		
AHI (n/h)	40.61 ± 12.02	15.01 ± 12.15	10.47 ± 15.38
Cumulative time under apnea and hypopnea (min)	86.30 ± 40.20	34.40 ± 36.31	25.78 ± 34.23
ODI (n/h)	38.72 ± 14.28	9.18 ± 13.21	8.17 ± 15.67
Snoring index (n/h)	244.26 ± 181.14	98.68 ± 115.43	65.81 ± 158.75
t90 (%)	8.85 ± 10.35	2.49 ± 11.47	3.94 ± 10.44
Arousal index (n/h)	23.68 ± 15.59	8.38 ± 16.51	1.23 ± 14.32

Notes: Clinical parameters: age, BMI; PSG-related parameters: AHI, ODI, complete time of apnoea and hypopnea (min), snoring index (n/h) (SI), oxygen desaturation index (n/h) (ODI), percentage of oxygen desaturation lower than 90% (t90) and total number of arousal events per hour (arousal index (n/h)).

Table 3 Correlation Between ISI Score and Each ISI Item and Δ PSG Parameter (Short-Term)

Δ PSG Parameter	ISI Preoperative	ISI 1	ISI 2	ISI 3	ISI 4	ISI 5	ISI 6	ISI 7
Δ AHI	r	-0.293	-0.013	0.155	-0.311	-0.053	-0.220	-0.152
	p	0.116	0.947	0.413	0.095	0.782	0.243	0.423
Δ Snoring index	r	-0.062	0.199	-0.081	0.152	0.254	0.088	0.224
	p	0.745	0.291	0.671	0.423	0.175	0.644	0.234
Δ Cumulative apnea hypopnea time	r	-0.212	-0.032	-0.107	-0.245	0.124	-0.100	-0.045
	p	0.260	0.866	0.574	0.191	0.513	0.598	0.815
Δ ODI	r	-0.341	0.009	0.158	-0.338	-0.086	-0.177	-0.093
	p	0.065	0.963	0.405	0.068	0.653	0.349	0.626
Δ t90	r	0.077	0.070	-0.041	-0.174	-0.060	-0.179	-0.138
	p	0.686	0.715	0.831	0.359	0.754	0.343	0.467
Δ Arousal index	r	-0.267	-0.212	-0.135	-0.226	-0.280	-0.181	-0.139
	p	0.154	0.261	0.476	0.230	0.134	0.339	0.463

Notes: Correlation between Δ PSG parameters such as Δ AHI, Δ snoring index, Δ cumulative apnea hypopnea time, Δ ODI, Δ t90, Δ arousal index and each item of the ISI questionnaire in the short-term follow-up.

Table 4 Correlation Between ISI Score and Each ISI Item and Δ PSG Parameter (Long-Term)

Δ PSG Parameter	ISI Preoperative	ISI 1	ISI 2	ISI 3	ISI 4	ISI 5	ISI 6	ISI 7
Δ AHI	r	-0.647*	-0.217	-0.038	-0.279	0.132	-0.178	-0.186
	p	0.004	0.386	0.880	0.262	0.602	0.479	0.460
Δ ODI	r	-0.693*	-0.106	0.024	-0.238	0.142	-0.124	-0.234
	p	0.001	0.677	0.925	0.341	0.574	0.624	0.350

(Continued)

Table 4 (Continued).

Δ PSG Parameter	ISI Preoperative	ISI 1	ISI 2	ISI 3	ISI 4	ISI 5	ISI 6	ISI 7
Δ Snoring index	r	-0.141	0.032	-0.216	0.104	0.404	-0.042	-0.104
	p	0.578	0.898	0.388	0.682	0.096	0.868	0.682
Δ Cumulative apnea hypopnea time	r	-0.411	-0.094	-0.180	-0.278	0.230	-0.026	-0.165
	p	0.090	0.710	0.474	0.264	0.359	0.917	0.512
Δ t90	r	-0.511	-0.143	-0.035	-0.315	0.092	-0.226	-0.184
	p	0.030	0.572	0.890	0.203	0.716	0.366	0.465
Δ Arousal index	r	-0.644*	-0.519	-0.425	-0.084	-0.102	-0.107	-0.076
	p	0.004	0.027	0.078	0.741	0.686	0.671	0.763

Notes: Correlation between Δ PSG parameters such as Δ AHI, Δ snoring index, Δ cumulative apnea hypopnea time, Δ ODI, Δ t90, Δ arousal index and each separate item of the ISI questionnaire in the long-term follow-up. *Bonferroni corrected significant correlations.

Discussion

We provide evidence for strong significant negative correlations between patient-reported scores to item one of the ISI questionnaire (i.e. difficulty falling asleep) and objective HGNS therapy outcome metrics such as the AHI, ODI and arousal index in long-term follow-up.

This is one of the first studies investigating the association between the different insomnia-related symptoms on PSG-related metrics. A strong negative correlation between preoperative difficulty falling asleep and important PSG-related metrics in the one-year follow-up could be shown. One possible explanation for this fact could be a reduced therapy compliance (reduced device usage) in patients suffering some specific insomnia-related symptoms. The co-occurrence of OSA and insomnia may impair OSA treatment by reducing compliance with PAP therapy.^{18,19} Further studies demonstrated especially insomnia-related symptoms associated with lower PAP therapy adherence.^{8,20} PAP adherence is reduced in patients with initial and late insomnia at baseline.²¹ Even if PAP adherence is reduced in patients suffering COMISA, insomnia-related symptoms are reduced under PAP therapy²¹ as well as under HGNS therapy.^{9,12,22} Insomnia symptoms are reported by up to 50% of patients suffering OSA and up to 40% patients suffering chronic insomnia also

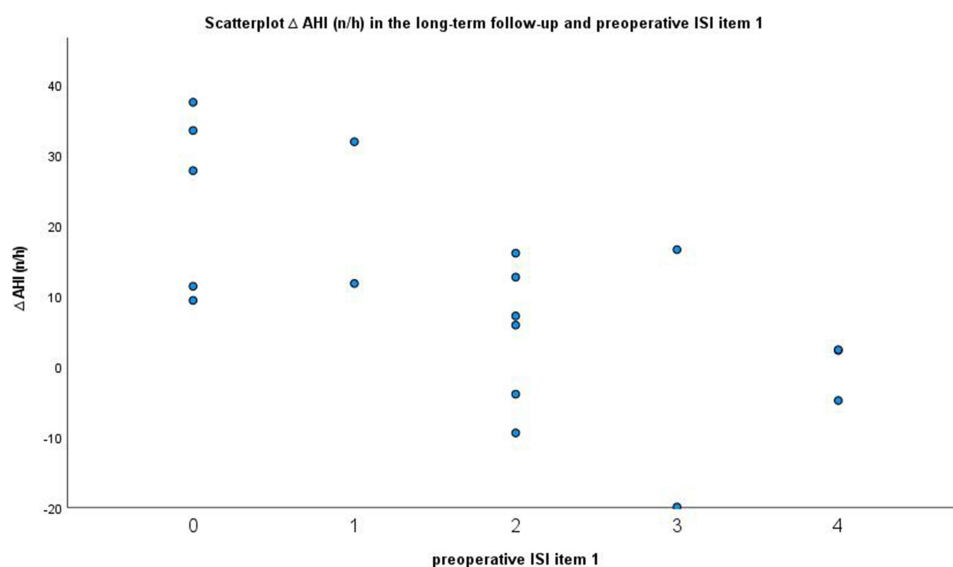


Figure 1 Scatterplot Δ AHI (n/h) in the long-term follow-up and preoperative ISI item 1.

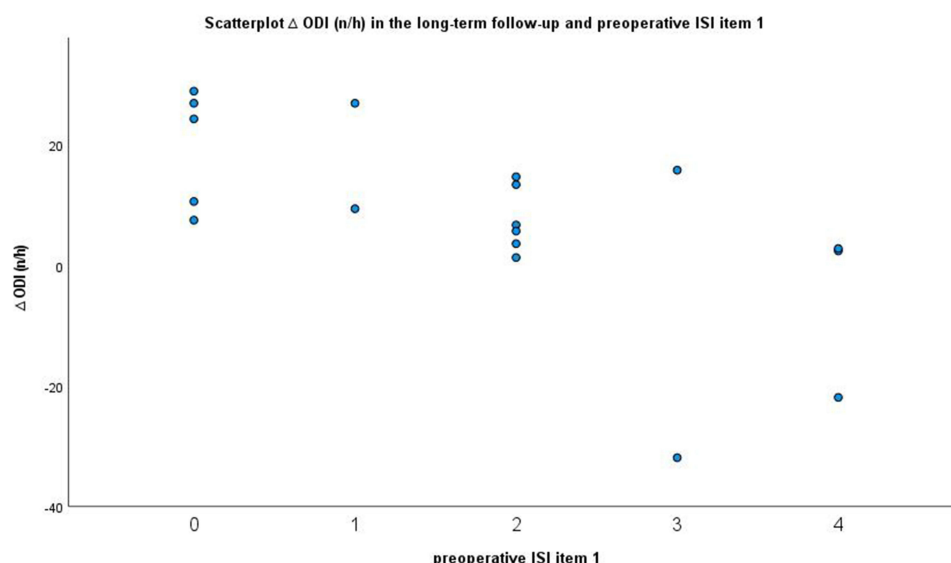


Figure 2 Scatterplot Δ ODI (n/h) in the long-term follow-up and preoperative ISI item 1.

meet the diagnostic criteria for OSA.⁸ PAP-intolerance is a key indication criterion for considering HGNS treatment. Therefore, patients who are HGNS therapy candidates may actually be patients with more pronounced insomnia-related symptoms. Adherence to HGNS therapy may therefore be higher in patients without comorbid insomnia. However, two studies investigated the effect of insomnia on the HGNS therapy adherence.^{12,23} Both reported no association between insomnia and HGNS therapy adherence. There was no significant difference between HGNS adherence in patients with OSA only compared to COMISA.²³ Furthermore, in the ADHERE registry no significant difference in therapy adherence between the group with preoperative ISI<15 and preoperative ISI>15 was observed.¹² However, a general reduction in HGNS-therapy adherence over time was observed.²⁴ This is a potential explanation of why a significant negative correlation was observed between preoperative difficulty falling asleep and important PSG-related metrics in the one-year follow-up but not in the short-term follow-up. Patients with increased difficulty falling asleep could therefore be more affected by reduced therapy adherence over time.

There are different studies investigating the impact of insomnia on the therapeutic outcome under HGNS therapy measured by PSG-related parameters^{9,12} as well as on patient-reported outcomes¹¹ and vice versa.²² However, the results are to date inconsistent. One study proved no significant difference in AHI reduction between a group with a preoperative ISI score <15 and a group with a preoperative ISI score >15.¹² Another study could prove a significant negative correlation between preoperative ISI score and postoperative AHI reduction in the short-term follow-up after three months.⁹

Most of the existing studies reported an improved ISI score under HGNS therapy. One study demonstrated a clinically relevant ISI score reduction in a higher percentage of those patients treated with a HGNS therapy compared to PAP therapy.²² A significant ISI score reduction under HGNS therapy in the short-term follow-up has been reported before.⁹ In the ADHERE registry all patients had an improved ISI score at follow-up visits ($p<0.001$). These patients with higher preoperative ISI scores showed a greater reduction in insomnia-related symptoms compared to those with lower preoperative ISI scores, ISI \geq 15 compared with ISI<15 ($p<0.05$).¹² The same study showed significant improvement for the ISI score and for each item in the ISI score from baseline to post-titration (PT) and baseline to final visit.¹² ISI was reduced by -7 ± 6.17 from baseline to the first PSG-based titration and by -8.06 ± 7.27 from baseline to final visit. These results are comparable to the results of our study. We are reporting here a preoperative ISI score of 18.67 ± 5.32 , a post-operative short-term ISI score of 12.7 ± 6.62 and a long-term post-operative ISI score of 10.08 ± 7.13 points. Furthermore, each item of the ISI score was improved from baseline to the first PSG-based titration post-titration with a further improvement post-titration to final visit.¹² Our study also showed an improvement in each item in the short-term follow-up with a further improvement in the long-term follow-up, except for item 3. Of note, our patients did not receive

any in-laboratory HGNS device titration during the PSG night. Therefore, our reported results may more closely depict the respective metrics at the patients' home.

The result of our study with greater improvement in insomnia-related symptoms with longer therapy seems to be counterintuitive to the result of more improvement of PSG-related parameters in the short-term follow-up compared to long-term follow-up in our study. This indicates that not only PSG-related parameters are associated with insomnia-related patient-reported outcomes. Previously, one study provided evidence that cognitive behavioural therapy combined with PAP is superior to PAP alone on insomnia-related outcomes.²⁵ Other authors showed an improvement in PAP therapy adherence and insomnia-related symptoms in patients suffering COMISA under cognitive behavioural therapy for insomnia.²⁶ We therefore suggest that comorbid insomnia in OSA patients under consideration for or after HGNS implantation should gain more attention. Further studies, especially investigating the added value of any additional behavioural therapy for patients suffering comorbid OSA and insomnia under HGNS therapy, may provide clinical insight on this important issue.

Limitations

Relevant limitations of our study are the relatively small sample size and the retrospective nature of this study. However, a sufficient post-hoc power of 0.87 for the correlation coefficient between question one of the ISI questionnaire and Δ AHI (r : -0.65) in the long-term follow-up and a post-hoc power of 0.93 for the correlation coefficient between question one of the ISI questionnaire and Δ ODI (r : -0.70) in the long-term follow-up were calculated. Furthermore, not all patients filled out the ISI questionnaire in the long-term follow-up. Data on therapy adherence were not available. Therefore, a possible association between difficulty falling asleep and therapy adherence cannot be proven, based on our available data. However, the gained data are of high quality and provide new information about the therapeutic outcome of patients treated by HGNS.

Conclusion

To the best of our knowledge this is one of the first studies investigating the association between the different separate insomnia-related symptoms on PSG-metrics in patients undergoing HGNS implantation. A strong significant correlation between question one of the ISI questionnaire (difficulty falling asleep) and both Δ AHI (r : -0.65 , $p=0.004$) and Δ ODI (r : -0.7 ; $p=0.001$) in the long-term follow-up could be shown. Difficulty falling asleep seems to be a significant and relevant clinical factor, associated with worse HGNS therapeutic outcome. Therefore, insomnia-related symptoms should be considered both at the time point of decision to implant a HGNS as well as postoperatively after implantation. Further studies are necessary to understand the impact of insomnia on HGNS therapeutic outcome and to investigate the potential benefits of further therapies, such as behavioral therapies, on HGNS therapeutic outcome in patients with PAP-intolerance suffering from COMISA.

Abbreviations

COMISA, coexistence of insomnia and obstructive sleep apnea; OSA, obstructive sleep apnea;

HGNS, hypoglossal nerve stimulation; CPAP, continuous positive airway pressure; PAP, positive airway pressure; PSG, polysomnography; ISI, insomnia severity index; AHI, apnea-hypopnea index; BMI, body mass index; DISE, drug-induced sleep endoscopy; ODI, oxygen desaturation index (n/h).

Ethics Approval and Consent to Participate

All patients provided informed consent to the use of their data for research purposes. The data were evaluated in a pseudonymized fashion. Only health data that are collected in the clinical routine were analyzed retrospectively. So-called "third parties" did not have access to the data and publication occurs exclusively in anonymized form. The Ethics Committee of the Rhineland-Palatinate Medical Association refrains from providing advice in such cases, citing the State Hospital Act (§36 and §37) (see also: <https://www.laek-rlp.de/ausschuesse-kommissionen/ethikkommission/>).

Data Sharing Statement

The data underlying this article cannot be shared publicly for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding authors.

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