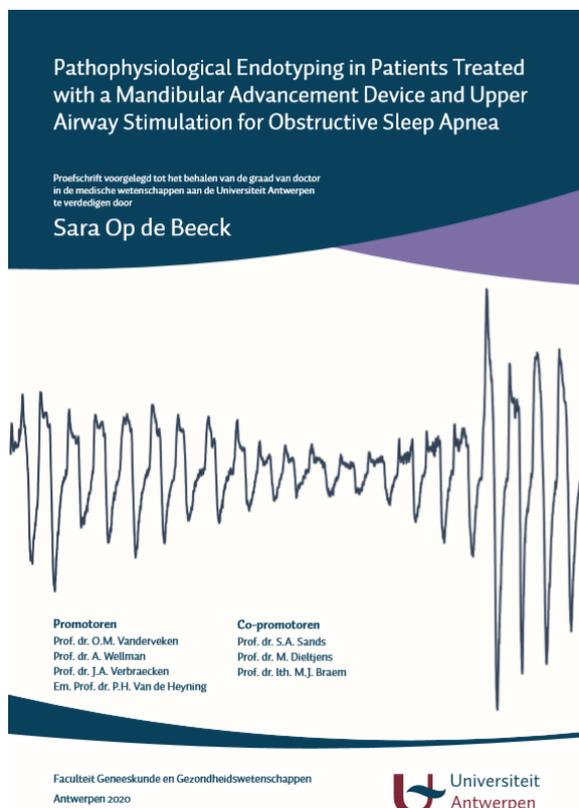# Articles of the Month – September 2020

Brilliant dissertation and thesis by Sara Op de Beeck, Universiteit Antwerpen, and the promotors, Professors Olivier Vanderveken, Johan Verbraecken, Andrew Wellman and Poul Van de Heyning.

She was fantastic in explaining loop gain and other complex breathing physiology variables that are becoming more and more important for the understanding of predictors of treatment success for non-CPAP therapies, such as oral appliances and upper airway stimulation. Below the cover of her thesis comes 3 of her articles, 2 from the thesis.

Pathophysiological Endotyping in Patients Treated with a Mandibular Advancement Device and Upper Airway Stimulation for Obstructive Sleep Apnea

Proefschrift voorgelegd tot het behalen van de graad van doctor in de medische wetenschappen aan de Universiteit Antwerpen te verdedigen door

Sara Op de Beeck

Promotoren
Prof. dr. O.M. Vanderveken
Prof. dr. A. Wellman
Prof. dr. J.A. Verbraecken
Em. Prof. dr. P.H. Van de Heyning

Co-promotoren
Prof. dr. S.A. Sands
Prof. dr. M. Dieltjens
Prof. dr. lth. M.J. Braem

Faculteit Geneeskunde en Gezondheidswetenschappen
Antwerpen 2020

Universiteit Antwerpen

Mandibular Advancement Device Treatment Efficacy is Associated with Polysomnographic Endotypes.

Op de Beeck S, Dieltjens M, Azarbarzin A, Willemen M, Verbraecken J, Braem M, Wellman A,
Sands SA°, Vanderveken OM° ° joint last authorship

ABSTRACT

Rationale: Mandibular advancement device (MAD) treatment efficacy varies among obstructive sleep apnea (OSA) patients.

Objectives: The current study aims to explain underlying individual differences in efficacy using OSA endotypic traits calculated from baseline clinical polysomnography: collapsibility (airflow at normal ventilatory drive, Vpassive), loop gain (drive response to reduced airflow), arousal threshold (drive preceding arousal), compensation (increase in airflow as drive increases) and the ventilatory response to arousal (VRA, increase in drive explained by arousal). Based on previous research, we hypothesized that responders to MAD treatment have a lower loop gain and milder collapsibility.

Methods: Thirty-six patients (apnea-hypopnea index [AHI] 23.5 [IQR:19.7 – 29.8]/h) underwent baseline and 3-month follow-up full polysomnography, with MAD fixed at 75% of maximal protrusion. Traits were estimated using baseline polysomnography according to Sands et al. (AJRCCM 2018). Response was defined as AHI reduction ≥ 50%.

Results: MAD treatment significantly reduced AHI (49.7% [23.9 – 63.6] of baseline, median [IQR]). Responders exhibited lower loop gain (mean [95%CI], 0.53 [0.48 – 0.58] vs. 0.65 [0.57– 0.73]; P = 0.020) at baseline compared to non-responders, a difference that persisted after adjustment for baseline AHI and BMI. Elevated loop gain remained associated with non-response after adjustment for collapsibility (OR: 3.03 [1.16 – 7.88] per 1 SD increase in loop gain [SD = 0.15]; P = 0.023).

Conclusions: MAD non-responders exhibit greater ventilatory instability, expressed as higher
loop gain. Assessment of the baseline degree of ventilatory instability using this approach may improve upfront MAD treatment patient selection.

==EADSM comment:==
Predictors for oral appliance therapy are urgently needed, initially and in the long run in order to avoid ineffective treatment and risks for unnecessary health consequences. A lot of research now concentrates on using PSG in new ways. This article highlights the importance of loop gain. Next article uses flow curves.

Predicting sleep apnea responses to oral appliance therapy using polysomnographic airflow

Daniel Vena [1], Ali Azarbarzin [1], Melania Marques [1,2], Sara Op de Beeck [3,4,5], Olivier M Vanderveken [3,4,5], Bradley A Edwards [6], Nicole Calianese [1], Lauren B Hess [1], Reza Radmand [1], Garun S Hamilton [7,8], Simon A Joosten [7,8], Luigi Taranto-Montemurro [1], Sang-Wook Kim [1,9], Johan Verbraecken [3,5], Marc Braem [3,10], David P White [1], Scott A Sands [1], Andrew Wellman [1]

ABSTRACT

Study objectives: Oral appliance therapy is an increasingly common option for treating obstructive sleep apnea (OSA) in patients who are intolerant to continuous positive airway pressure (CPAP). Clinically applicable tools to identify patients who could respond to oral appliance therapy are limited.

Methods: Data from three studies (N = 81) were compiled, which included two sleep study nights, on and off oral appliance treatment. Along with clinical variables, airflow features were computed that included the average drop in airflow during respiratory events (event depth) and flow shape features, which, from previous work, indicates the mechanism of pharyngeal collapse. A model was developed to predict oral appliance treatment response (>50% reduction in apnea-hypopnea index [AHI] from baseline plus a treatment AHI <10 events/h). Model performance was quantified using (1) accuracy and (2) the difference in oral appliance treatment efficacy (percent reduction in AHI) and treatment AHI between predicted responders and nonresponders.

Results: In addition to age and body mass index (BMI), event depth and expiratory "pinching" (validated to reflect palatal prolapse) were the airflow features selected by the model. Nonresponders had deeper events, "pinched" expiratory flow shape (i.e. associated with palatal collapse), were older, and had a higher BMI. Prediction accuracy was 74% and treatment AHI was lower in predicted responders compared to nonresponders by a clinically meaningful margin (8.0 [5.1 to 11.6] vs. 20.0 [12.2 to 29.5] events/h, p < 0.001).

Conclusions: A model developed with airflow features calculated from routine polysomnography, combined with age and BMI, identified oral appliance treatment responders from nonresponders. This research represents an important application of phenotyping to identify alternative treatments for personalized OSA management.

Keywords: OSA; oral appliance therapy; upper airway.

Phenotypic Labelling Using Drug-Induced Sleep Endoscopy Improves Patient Selection for Mandibular Advancement Device Outcome: A Prospective Study

Sara Op de Beeck [1], Marijke Dieltjens [2], Annelies E Verbruggen [3], Anneclaire V Vroegop [3], Kristien Wouters [4], Evert Hamans [5], Marc Willemen [6], Johan Verbraecken [7], Wilfried A De Backer [5], Paul H Van de Heyning [1], Marc J Braem [8], Olivier M Vanderveken [1]

ABSTRACT

Study objectives: Mandibular advancement device (MAD) outcome varies between patients. We hypothesized that upper airway collapse sites, patterns, and degrees assessed during baseline drug-induced sleep endoscopy (DISE) affect MAD outcome.

Methods: One hundred patients with obstructive sleep apnea (OSA) were included and underwent baseline type 1 polysomnography. MAD was fitted intraorally at fixed 75% maximal protrusion. A total of 72 patients completed 3-month follow-up polysomnography and baseline DISE. Response was defined as apnea-hypopnea index (AHI) reduction ≥ 50%, deterioration as AHI increases during MAD treatment compared to baseline.

Results: Adjusting for baseline AHI and body mass index, patients with tongue base collapse showed 3.69 higher odds (1.27-10.73; P = .0128) for response. Complete concentric collapse at the level of the palate (5.32 [1.21-23.28]; P = .0234) and complete laterolateral oropharyngeal collapse (6.62 [1.14-38.34]; P = .0330) related to deterioration. Results for tongue base collapse and complete concentric collapse at the level of the palate were confirmed in the moderate to severe OSA subgroup. Applying these results to this selected subgroup increased response rate with 54% and decreased deterioration rate with 53%. These results were confirmed using other response and deterioration definitions.

Conclusions: Three baseline DISE phenotypes identified during drug-induced sleep were significantly related to MAD treatment outcome: one beneficial, tongue base collapse, and two adverse, complete concentric collapse at the level of the palate and complete laterolateral oropharyngeal collapse. If confirmed in future prospective studies, these results could guide patient selection for MAD outcome.

EADSM comment:
For centers who can perform DISE, these predictors based on type of collapse are clear. Concentric collapse and lateral collapse relate to non-response with MAD.

Identifying the Predominant Site of Upper Airway Collapse in Obstructive Sleep Apnoea Patients Using Snore Signals

Arun Sebastian, Peter A Cistulli, Gary Cohen, Philip de Chazal

ABSTRACT

Knowledge regarding the site of airway collapse could help in choosing an appropriate structure-specific or individualized treatment for obstructive sleep apnoea (OSA). We investigated if the audio signal recorded during hypopnoea (partial obstruction) events can predict the site-of-collapse of the upper airway. In this study, we designed an automatic classifier that predicts the predominant site of upper airway collapse for a patient as "lateral wall", "palate", "tongue-based" related collapse or "multi-level" site-of-collapse by processing of the audio signal. The probable site-of-collapse was determined by manual analysis of the shape of the airflow signal during hypopnoea, which has been reported to correlate with the site of collapse. Audio signal was recorded simultaneously with full-night polysomnography during sleep with a ceiling microphone. Various time and frequency features of the audio signal were extracted to classify the audio signal into lateral wall, palate and tongue-base related collapse. We introduced an unbiased process using nested leave-one patient-out cross-validation to choose the optimal features. The classification was carried out with a multi-class linear discriminant analysis classifier. Performance of the proposed model showed that our automatic system can achieve an overall accuracy of 65% for determining the predominant site-of-collapse for all site-of-collapse classes and an accuracy of 80% for classifying tongue/non-tongue related collapse. Our results indicate that the audio signal recorded during sleep can be helpful in identifying the site-of-collapse and therefore could potentially be used as a new tool for deciding appropriate treatment for OSA.

EADSM comment:
Interesting new methodology in order to identify the site of pharyngeal collapse based on snoring signals, seems to be an existing step forward towards the simplification of finding good candidates for non-CPAP therapies.

Maximum voluntary retrusion or habitual bite position for mandibular advancement assessment in the treatment of obstructive sleep apnoea patients

Daniela Rita Ippolito [1], Chiara Stipa [1], Matteo Cameli [2], Giovanni Sorrenti [3], Irene Pelligra [3], Giulio Alessandri-Bonetti [1]

ABSTRACT

Background: There is no consensus on whether the range of mandibular advancement for the construction of mandibular advancement devices in obstructive sleep apnoea (OSA) patients should be measured from a starting position of maximum voluntary retrusion or habitual bite position.

Objective: The purposes of this study were to investigate the differences in mandibular advancement registrations starting from maximum voluntary retrusion or from habitual bite position and to evaluate the reliability of these assessments.

Methods: A retrospective cohort analysis of 126 patients with OSA was performed. All patients had their mandibular range of motion evaluated twice (starting from maximum voluntary retrusion and from habitual bite position) through the George Gauge before undergoing drug-induced sleep endoscopy. The Dahlberg formula and paired t test were used to calculate random and systematic errors of dental positions assessment. Test-retest reliability was quantified using the intra-class correlation coefficient (ICC).

Results: The mean mandibular range starting from maximum voluntary retrusion and from habitual bite position were 12.49 ± 2.19 mm and 7.68 ± 2.29 mm, respectively, with a mean distance between the two starting positions of 4.81 ± 1.75 mm. No systematic error was found (P > .05), and random errors ranged from 0.30 to 0.95 mm. ICC values were excellent for maximum voluntary protrusion (ICC = 0.986) and maximum voluntary retrusion (ICC = 0.956), whereas habitual bite position showed a good value (ICC = 0.818).

Conclusion: The difference between maximum voluntary retrusion and habitual bite position is potentially relevant. Maximum retrusion is advisable as starting point of the mandibular advancement registration since it provides a more reliable measure.

EADSM comment:
Important study about the way we measure the degree of mandibular advancement. Using a gauge and a percentage measurement may lead to a large difference compared to measuring from central occlusion, since the mandible slides backwards during opening. This phenomenon was already highlighted by Anette Fransson 2003, but seems to often have been forgotten in studies reporting the degree of advancement and how it was measured.
Fransson AM, Tegelberg A, Svenson BA, Wenneberg B, Isacsson G. Validation of measurements of mandibular protrusion in the treatment of obstructive sleep apnoea and snoring with a mandibular protruding device. Eur J Orthod. 2003 Aug;25(4):377-83. doi: 10.1093/ejo/25.4.377. PMID: 12938844.