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Obstructive sleep-disordered breathing and orthodontics. An interview with Christian Guilleminault, Michèle Hervy-Auboiron, Yu-Shu Huang and Kasey Li*

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N.D.R. The implementation of this interview was mourned by the departure of Christian Guilleminault, during the correction phase of the print orders.

Prof. Christian Guilleminault is the author or co-author of 13 books and has published over 826 articles in peer-reviewed journals. He has lectured in most countries and has received 37 awards and honours for his contributions to neurology, sleep disorders and sleep medicine in the US and from international organisations.

In 1963, Christian Guilleminault passed the competitive examination to become an intern at the Hôpitaux de Paris. He began his first research projects at the Foch Hospital and the Orsay Faculty of Sciences. After passing his thesis in 1968, as a young Doctor of Medicine, he began his work on sleep pathologies. He trained in neurology mainly at the Salpêtrière Hospital in Paris and, after completing his studies in neurology, he became a Doctor of Medicine.

He trained in psychiatry in Geneva and Paris. He obtained a diploma of advanced study from the Faculty of Sciences of the University of Paris (histology and histochemistry) and was certified in neurology and psychiatry in 1970. He was appointed Senior Scientist at the National Institute of Health and Medical Research (INSERM) in Paris in 1977.

He obtained the Habilitation to direct research (HDR) from the Faculty of Medicine of the University of Montpellier in 1998, and a PhD in Biology/Neurosciences from the University of Grenoble in 1999.

He was appointed Associate Professor of Psychiatry and Behavioural Sciences at Stanford University in 1980, and then Full Professor of Neurology in Psychiatry, Department of Psychiatry and Behavioural Sciences and (Courtesy) Neurology, Stanford University School of Medicine in 1985. Visiting Professor at the University of Marburg (Germany) and recipient of a Humbolt Fellowship in 1987-1988, he was also Professor without tenure at the Montpellier Medical School in 1994-1996.

Currently, he is a Professor in the Department of Psychiatry and Behavioral Sciences and, by courtesy, in the Department of Neurology at Stanford University School of Medicine and a Full Professor in the Division of Sleep Medicine at Stanford University. He is a member of the American Electroencephalographic Society and the American Academy of Sleep Medicine (AASM).

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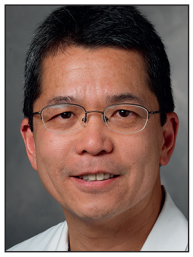
Dr. Michèle Hervy-Auboiron is a doctor of dentistry and a qualified specialist in orthodontics. She holds a Certificate of Special Clinical Studies in Orthodontics, a University Diploma in Occlusodontology, a University Diploma in Maxillofacial and Oral Expertise and an Inter-University Diploma "Sleep and pathologies". She regularly collaborates and publishes[30,77,119] with Christian Guilleminault.

Prof. Yu-Shu Huang graduated from Chang Gung University in Taiwan. She trained in psychiatry and pediatrics at Chang Gung Memorial Hospital. She also trained in sleep medicine at the Stanford Sleep Center in 2003, under the supervision of Professor Christian Guilleminault. She then completed her PhD at the Faculty of Medicine of the University of Lisbon. Her clinical and research interests are in pediatric psychiatry and sleep medicine. She has published more than 100 articles in peer-reviewed journals, including paediatric hypersomnia, narcolepsy, obstructive sleep apnea in paediatrics and attention deficit disorder with or without hyperactivity (ADHD). She is a professor in the department of child and adolescent psychiatry.

She is currently Director of the Department of Child and Adolescent Psychiatry at Chang Gung Memorial Hospital in Taipei, Taiwan. She is currently also the Director of the Department of Child and Adolescent Psychiatry at Chang Gung Memorial Hospital.



Dr. Kasey Li has a long academic and professional career. Specialising in the treatment of obstructive sleep apnoea, Dr. Li is the only surgeon in the world to be certified by three American Boards: the American Boards of Otolaryngology, Oral and Maxillofacial Surgery, and Facial Plastic and Reconstructive Surgery. Based on his unique background and experience, he has developed and refined many surgical techniques for sleep apnea. Dr. Li is the surgical consultant for many sleep disorder treatment centres, including the Stanford Sleep Disorders Clinic's multidisciplinary sleep treatment team. He has published more than 100 scientific articles and book chapters on sleep apnea surgery and maxillofacial surgery. By invitation, Dr. Li has lectured extensively in the United States and abroad as an internationally recognized expert in sleep apnea surgery.

Philippe Amat: *The relationship between sleep medicine and orthodontics is a subject of constant interest for our disciplines, as shown by the programmes of their respective congresses and the many publications devoted to them over the last thirty years. We would like this interview to provide our readers with a summary of some of the key elements of this relationship and to shed light on the many facets of your important contributions to the creation and development of "sleep medicine" as a new field of medicine throughout the world.*

Christian Guilleminault, Michèle Hervy-Auboiron, Yu-Shu Huang, Kasey Li: We are pleased to answer the questions in this interview in order to provide the readers of the Orthodontie Française with a summary of the various medical dimensions of sleep disorders and the contribution of orthodontics to their treatment. We also welcome this initiative by the Orthodontie Française to bring together in a special issue, almost a monograph, most of the current data on the interrelationship between obstructive sleep disorders and orthodontics.

1. Your academic background

Philippe Amat: *Professor Guilleminault, in December 2013 you gave an interview[74] to the Sud-Ouest newspaper in which you spoke of the scepticism that greeted your first research in France. You declared: "Nobody believed in it. In France, I was an idiot. Considered naive. My career, when I was a young and curious neurologist, was blocked". Is this the reason why you decided to accept the position of assistant professor in the Department of Psychiatry and Behavioural Sciences at Stanford, which William Charles Dement offered you in 1971, in Bruges, during an international congress on sleep?*

Christian Guilleminault: Certainly, it was an opportunity for me to progress in my research. In Paris, my boss allowed me to continue my research, but without giving me the time or the budget. I was forced to carry out nightly examinations of patients, electrocardiograms, electroencephalograms, breathing, muscles and movements at my own expense. My management had told me that "sleep is for dreamers". So I worked day and night and paid for the electrodes needed for the recordings. This allowed me to consider a thesis. I observed respiratory disorders in ordinary people, non-obese children. I observed periodic breathing but nobody believed it.

PA: *You said[74] "I came to California with my 450 recordings and my files". What resources did you have at Stanford?*

CG: A few months after the Bruges International Congress, I moved to California and took up a position as assistant professor in the Department of Psychiatry and Behavioural Sciences at Stanford. My research was able to develop more easily thanks to the means at my disposal. In addition to an office, a laboratory and funding, I was able to gather a team of researchers at my side.

PA: *Before you went to Stanford, you had opened the first sleep laboratory in Paris in 1970. Why did you become interested in what was to become sleep medicine?*

CG: At the time, snoring and night-time breathing problems were attributed to the very obese who suffered from hypersomnia: the Pickwick syndrome, named after the character in a novel by Charles Dickens, described in 1956.

I was convinced that apnoea syndrome can affect anyone, causing various disorders: hypertension, cardiac arrhythmias, exhaustion. In non-obese children, brought to consultation for attention or memory problems, hyperactivity, enuresis or sleepwalking, I had diagnosed sleep apnoea.

PA: *Our daily clinical practice has convinced us that, while the evidence-based approach[3] is a good guide, it can also become a bad teacher. In an interview[136], Prof. J.-D. Orthlieb had stigmatised the utopian aspect of evidence-based medicine and pointed out the risk that it would promote "a new form of scholastic ostracism". He said: "By its clarity and rigour, deductive reasoning appears at first sight as the essential instrument of scientific progress. But, in an incomplete science that is being created and that is progressing, L. de Broglie asserts that inductive reasoning is the true source of great scientific progress. It is necessary to leave room for both the necessary reason and the indispensable freedom of the imagination. Thus observation, the luminous idea, obvious in itself, will enlighten. Then, rigorous experiment will instruct and validate".*

Since 1972 and your first publications on sleep apnoea[42,43,67], your career as a clinician, researcher and teacher seems to show that you have not taken account of fixed opinions, academic and administrative blockages. What is your approach to scientific research?

CG: Research is indeed dual, inductive and deductive. I would like to stress that a methodologically rigorous demonstration through randomised double-blind clinical trials over a sufficiently long period of time is always necessary before we can say that a therapy is effective and what the possible complications are, and this is too often not done. The constant aim of medical research is to help improve the health of patients and requires great determination on the part of the researcher, as you have mentioned. It also requires curiosity, open-mindedness, scientific rigour and the ability to bring together and share knowledge.

PA: *Michèle, we met at the University Diploma of Occlusodontology of Paris V directed by Claude Michel Valentin. Can you describe the rest of your univer-*

sity career and the motivations behind your choice of post-graduate training?

Michèle Hervy-Auboiron: It was precisely during this DU that I became interested in sleep apnea-hypopnea syndrome (SAHOS). At the time, the mandibular advancement orthoses were beginning to become a therapeutic alternative of choice and Bernard Fleiter had suggested that I focus my dissertation on their potential side effects, and even on proposals to reduce them. On the judicious advice of Alain Lautrou, I worked on a more functional project. Subsequently, CG recommended that I take the DIU Sleep and Pathology, in order to deepen my general knowledge of the subject

PA: *When we met, I often witnessed the constant and friendly complicity between you and Christian Guilleminault. Under what circumstances did you meet and how did you come to work together?*

MH-A: I had developed a medical device for functional rehabilitation: the SomNyx®, which was the winner of the OSEO Emergence competition in April 2012. Friends of mine who are ENT specialists, including Frederic Chalumeau, asked me to accompany them to San Francisco for the American Thoracic Society conference and they asked CG to meet them at Stanford. CG was totally on board with the treatment plan. He immediately considered two studies, one in children in Taiwan and one in adults in France and Canada. We couldn't have asked for better support. The complicity you mention reflects both a sincere friendship and a deep respect.

PA: *Professor Yu-Shu Huang, you have completed your academic training in three continents, at Chang Gung University in Taiwan, the Stanford Sleep Center and the University of Lisbon Medical School. Can you share with our readers the key elements of your educational choices and your current clinical and research interests?*

Yu-Shu Huang: I completed my training in psychiatry and pediatrics at Chang Gung Memorial Hospital. In 2000, Chang Gung Memorial Hospital opened the largest sleep centre in Asia and I was asked to go to Stanford University to learn sleep medicine from Professor Guilleminault. Back in Taiwan, I continued to work with Professor Christian Guilleminault on sleep medicine studies. In particular, I undertook research on paediatric attention deficit hyperactivity disorder (ADHD) and obstructive sleep apnea (OSA).

In addition, together with Professor Guilleminault, I have published numerous studies on paediatric hypersomnia (Kleine-Levin syndrome) and narcolepsy. In 2012, Professor Guilleminault thought that there were important correlations between premature babies and sleep apnoea. So he suggested I go to the University of Lisbon to specialise in sleep medicine. Professor Teresa Paiva had agreed to direct my PhD thesis and she proposed the topic "Premature babies and sleep-disordered breathing in children". Therefore, my main interest today is in paediatric sleep medicine, with a focus on paediatric sleep apnoea and paediatric hypersomnia.

PA: *You are currently Professor in the Department of Child and Adolescent Psychiatry at Chang Gung Memorial Hospital in Taipei, Taiwan. What differences have you observed as a teacher, and previously as a student, between Taiwan, the US and Europe?*

Y-SH: You are right to mention these differences. Yes, in Taiwan, the US and Europe, the situation is different, not only for the teachers but also for the students. In Taiwan, the students, especially the medical students, who are usually very good students who have made it to medical school, are more passive during their studies. During lectures they are always quiet and are rarely asked to speak. Very few students will proactively ask questions, as they see their teacher as the authority. Taiwanese students usually lack self-confidence and a global outlook. The teachings of Taiwanese teachers are also traditional and rely on the use of textbooks. There is also less opportunity for teachers and students to interact after class.

In the United States, it is open education. The distance between teachers and students is smaller. Students are strongly encouraged to ask many questions in class. The relationship between teachers and students is sometimes like a camaraderie. I was not used to it at the beginning.

In many European countries, I have felt the strength of tradition and the influence of a rich

historical past. The relationship between students and teachers is halfway between those I experienced in Taiwan and the United States. The students' learning attitude is active and polite towards the teachers. But students and teachers respect each other. The pervasiveness and weight of historical culture is probably the most important difference between Europe and the US.

PA: *Kasey, you are the only surgeon in the world certified by the American Boards of Otolaryngology, Oral and Maxillofacial Surgery, and Facial Plastic and Reconstructive Surgery. Can you tell our readers about the key stages of your academic career?*

Kasey Li: My father was an ear, nose and throat specialist, but I decided to study dental surgery. I first graduated from UCLA dental school and then spent a year doing research. I then enrolled in the Oral and Maxillofacial Surgery Residency Program at Harvard, where I also earned a medical degree. Immediately after completing my oral surgery training, I entered the otolaryngology/head and neck surgery program at Harvard. After spending a decade in Boston, I returned to California and did a fellowship in facial plastic surgery before coming to Palo Alto where I met the hard-headed Frenchman.

PA: *When did you first meet Christian Guilleminault? What projects did you carry out together and to which you dedicated publications?*

KL: I first met Christian in 1997 when I started practicing at Stanford. Because of my training, it was natural to start working closely with him. We started the multidisciplinary treatment clinic in 1998 at the Stanford Sleep Clinic, which was called the Friday Clinic. It was every Friday afternoon between 1 pm and 4:30 pm and we had wine and cheese with the colleagues afterwards. Of course Christian drank all the wine because I didn't! It was a good time and I have fond memories of it. We discussed a lot of treatment options and presented alternatives to CPAP. We received many families with parents and their children at the same time. All my sleep publications were with Christian and they covered 90% of my academic work.

2. From obstructive sleep apnea syndrome to upper airway resistance syndrome

PA: *Christian Guilleminault, the readers of French Orthodontics know you through your conferences, publications and books. You are one of the founding fathers of sleep medicine, you created the first sleep laboratory in Paris in 1970 and after defining the obstructive sleep apnea syndrome[42,43,67], you have and continue to publish an amazing volume of research. Since the description of "Pickwick's syndrome"[10], what have been the key milestones in the recognition of obstructive sleep apnoea syndrome (OSA) in non-obese adults and in children?*

CG: The subject is vast. Decades of research and questioning have led to the recognition of obstructive sleep apnea syndrome in adults and children. After Bickelmann, *et al.*[10] proposed the name "Pickwick syndrome", the German school was the first to register these obese subjects

The results of this study were used to identify "Pickwickian" sleep patterns and to show the presence of "obstructive apneas" during sleep.

In 1962, Werner Gerardy, *et al.*[38] found "repeated obstructive apnoea" on polygraphic recordings of two obese patients and a return to normal breathing with significant snoring associated with tachycardia. Kuhn[90] (Kuhlo after his name change) continued this early work and ensured the international dissemination of their results. The therapeutic success of tracheotomy[97], which he was the first to perform in a Pickwickian, demonstrated that sleepiness was related to sleep fragmentation caused by apnoea.

Other researchers, such as Gastaut and Lugaresi[129], have complemented the work of the German school by studying the cardiovascular events occurring during sleep apnea in obese Pickwickians.

Organised in 1972 in Italy by Lugaresi and Sadoul, the "Hypersomnia and Periodic Breathing" symposium was the first international meeting where sleep apnoea was the focus of debate. William C. Dement from Stanford University was invited and had little knowledge of the topic and asked me to represent him. I presented the evidence that sleep

apnoea was not exclusive to obese Pickwickians but could be seen in normal weight patients[42].

The term "obstructive hypopnea" originated from the observation by Londsdorfer, Kurtz[98] and Krieger[96] that upper airway obstruction could be incomplete and still induce arousal responses on the electroencephalogram.

The polygraphic recordings of B. Duron[35] allowed him to dissociate obstructive, mixed and central apnoeas.

Finally, in order to assert the existence of a syndrome independently of an association with obesity, with WC. Dement, we proposed[67] the entities "sleep-apnea-syndrome", and "obstructive sleep-apnea-syndrome (OSAS)".

PA: *How did polysomnographic studies and the use of an oesophageal pressure probe then lead you to the description of abnormal upper airway resistance in the child[52,61,64,68]?*

CG, MH-A, Y-SH, KL: We had accumulated paediatric case reports and demonstrated that OSAS can cause multiple complications[53]. We described children with clinical signs and symptoms similar to those seen in sleep apnoea without any apnoea or hypopnoea on the nocturnal polygraph recording. In the 1982[68] publication you quoted, it was indeed by measuring respiratory effort with an oesophageal pressure probe that, in these children, we identified increased respiratory effort as the only abnormal element in the recording. We described the multiple symptoms of this abnormal resistance of the upper airways, without any real impact on oxygen saturation, but associated with repeated disturbances of the electroencephalogram (EEG) during sleep.

Y-SH: Polysomnography (PSG) is used to monitor abnormal upper airway resistance, including nasal cannula pressure transducer, oral thermistor, chest and abdominal bands (RIP belts), pulse oximetry, neck microphone and Intercostal EMG (ICR). Esophageal pressure (EP) is not routinely monitored, but will be useful in doubtful cases.

Historically, "hypopnea" was defined at a time when breathing at the nose and mouth was monitored by thermistors that measured temperature changes and with an oximeter of limited accuracy. The definition of hypopnoea (hypopnoea can be assessed with a 3% drop in SaO2 or a micro-awakening of 3 seconds or more on the electroencephalogram (EEG)), which is still sometimes used, is related to these recording difficulties. But now we have the "nasal cannula pressure sensor", we have a better oximeter, and we know that cortical disorders related to abnormal breathing are important consequences of the problem.

PA: *What clinical consequences of this abnormal upper airway resistance have you identified on children's attention, memory, academic performance and daytime hyperactivity?*

CG, MH-A, Y-SH, KL: We had described the multiple symptoms[68], in particular inattention, daytime hyperactivity, impact on memory, school results, clinical consequences of this abnormal upper airway resistance. Since this 1982 publication, other research work has been carried out. They show that sleep-disordered breathing can affect the physical and mental health of children, with growth disturbances, cardiac and metabolic problems.

Studies of children with OSA and attention deficit hyperactivity disorder (ADHD), published in 2004[76] (Journal of Sleep Research) and 2007[81] (Sleep Medicine Journal), also showed that in children with OSA treated with adenotonsillectomy, ADHD symptoms improved significantly.

KL: Christian had great clinical acumen and had built up so much experience that he could see things and understand things that others could not. I would only report that in the early days of High Resistance Upper Airway Syndrome, colleagues would come on stage and openly mock Christian with a fake French accent! Of course not, this didn't bother Christian. He continued his research, describing multiple hitherto unknown paediatric symptoms, helping so many children that others had simply dismissed!

PA: *Your investigations in adolescents and adults have led to the description of Upper Airway Resistance Syndrome (UARS)[63,65,165,166]. What is the clinical picture, what are the main consequences, including cardiac and*

cognitive consequences, and why are patients with HVAS still sometimes undiagnosed and untreated[138]?

CG, MH-A, Y-SH, KL: Initial ignorance of the possibility of abnormal upper airway resistance in children may have been due to the lack of use of an oesophageal probe in polysomnographic studies in most laboratories. We continued our studies and extended their initial scope from children to adolescents and adults. The accumulation of our observations led us to the description of a clinical picture in adults, which we published under the name of "high resistance syndrome of the upper airways"[62]. We showed that this HVAS was associated with snoring and had numerous consequences, notably cardiac and cognitive. Since then, the introduction of nasal cannulae with pressure recording has meant that we are no longer routinely required to use esophageal pressure recording to study airflow limitations.

There is no gender predominance in SHRVAS. Subjects are generally non-obese, with a body mass index (BMI) ≤ 25kg m^2, and often younger than OSA patients.

Patients with ARVHS experience daytime sleepiness or fatigue, and have impaired cognitive function and even heart rate instability. We have shown that their symptoms overlap with those of OSA patients, with their own characteristics[41]. In them, chronic insomnia tends to be more frequent, sometimes with night-time awakenings and difficulty in returning to sleep. They often complain of sleep insomnia and maintenance insomnia, thought to be due to "conditioning", because of frequent sleep disturbances[57]. Parasomnias such as somnambulism and sleep terrors, myalgia, depression and anxiety have also been reported.

Despite the difference in clinical features, it is sometimes difficult to distinguish patients with ARVAS from those with mild OSAS, based on symptoms and clinical signs alone. The diagnosis can only be confirmed by polysomnography. Nocturnal PSG shows no apnoeas or hypopnoeas and respiratory abnormalities consist of periods of increased respiratory effort, fragmentation of sleep, presence of micro-arousals associated with a high resistance event and flattening of the respiratory curve, indicating airflow limitation.

It should be noted that ARVHS can frequently be misinterpreted as chronic fatigue syndrome, fibromyalgia, or psychiatric disorders such as attention deficit disorder with or without hyperactivity (ADD/ADHD)[107].

PA: *In 2018, you wrote that the terms Upper Airway Resistance Syndrome, Obstructive Sleep Apnoea Syndrome and Hypopnoea Apnoea Index are only historical[7]. You recalled that we now have a better understanding of the development of sleep-disordered breathing and its evolution with age, leading to comorbidities. You pointed out that our current knowledge is now sufficient to go beyond these definitions, to recognise the problems differently, much earlier, and to prevent the factors leading to sleep-disordered breathing. Can you explain how the recognition of non-hypoxic sleep-disordered breathing[45] is a step in this direction?*

CG, MH-A, Y-SH, KL: Indeed, upper airway resistance syndrome (UARS), known as obstructive sleep apnoea syndrome (OSA), was described as abnormal breathing during sleep, based on recording technology and knowledge at the time. Although the definition of these terms has advanced sleep medicine, they are less useful today. Historically, the definition of SHRVAS was intended to recognise those conditions not covered by "OSA" and to encourage specialists to recognize conditions earlier and to prompt research into the developmental characteristics of sleep-disordered breathing (SDB). The technology used to monitor SDB has changed over time, resulting in different, but not necessarily better, recognition of SDB.

Sometimes, patients are not diagnosed with sleep-disordered breathing or obstructive sleep apnoea until they are 40 years old. This is unfortunate, as SDB at this age is accompanied by various comorbidities, including excessive daytime sleepiness, increased risk of traffic accidents and cardiovascular complications. The real issue is therefore to recognise the problems much earlier and to understand what can be done to prevent their development.

By analysing different patterns of abnormal breathing (Fig. 1) such as flow limitations, mouth breathing, changes in inspiration and expiration times, chest and expiratory muscle activity, snoring sounds, etc., it is possible to recognise cases of

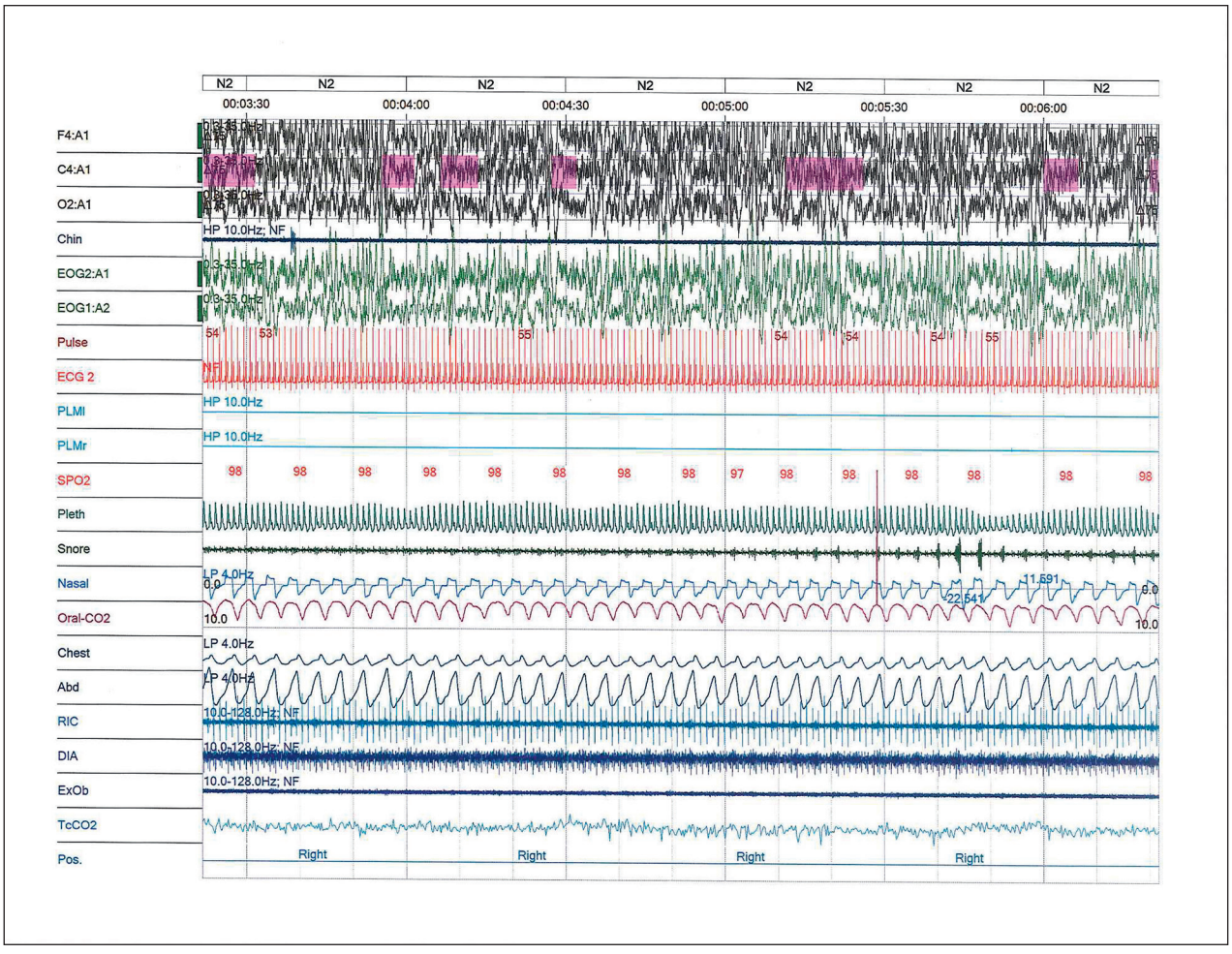


Figure 1

Monitoring of oral respiration. The Oral-CO2 channel (15th from the top) indicates continuous mouth breathing. Here it is associated with flow limitation and snoring develops after mouth breathing. According to Christian Guilleminault, some EEG indicators (including the CAP –cycling alternating pattern– which is an EEG marker of sleep instability) present in patients with SHRVAS (pink fluorescent areas on the C4:A1 EEG channel) are too often ignored, although they testify to the impact of any flow limitation on sleep quality and its consequences on cognitive performance.

"non-hypoxic" sleep disorder. By going beyond the traditional notions of apnoea-hypopnoea and hypoxic sleep disordered breathing, which are still favoured by clinical practice guidelines, we can avoid delaying the treatment of these children and prevent the progression of their SDB.

PA: *Obstructive sleep-disordered breathing (OSDB) is associated with increased respiratory effort, of which oesophageal pressure is the gold standard, but it is generally poorly tolerated because of its invasiveness. You have shown[70] that a machine learning computer technique can be used as a tool to quantify respiratory effort from routinely collected non-invasive polysomnography measurements without the need for oesophageal pressure. What are the future prospects for this technique and for OSDB diagnosis more generally?*

CG, MH-A, Y-SH, KL: Yes, we can now use Artificial Intelligence (AI) as the self-learning computer program ("machine learning", "deep learning"). Computers are given the ability to "learn" from data, i.e. to improve their performance in solving tasks without being explicitly programmed for each one. The use of AI can help us with some difficult interpretations of PSG, such as quantifying respiratory effort, or to build some predictive models.

PA: Numerous sleep analysis applications for smartphones provide data on sleep patterns, but none of them have been successfully validated by polysomnography to date[127,135]. Applications to assist in self-care sleep management have also been developed but their reliability has not been addressed due to a lack of validation studies[28].

Can we expect an increase in the sensitivity and specificity of these applications compared to polysomnography, which would profoundly change the management patterns of SDB?

CG, MH-A, Y-SH, KL: There are currently many sleep application programs, most of which are primarily developed using heart rate, pulse and respiration. But "breathing" is a complex function involving different anatomical regions such as the nose, mouth, chest, abdomen and brain. Breathing is controlled by different parts of the brain, including the brainstem and cortical regions. The relationship between "breathing, heart and brain" is therefore particularly complex and dynamic. This is the limitation of the applications currently available for download. If these programs could increase the signal or information from the brain, their reliability should increase.

3. OSDB for children, adolescents and adults

PA: *Dr. Olivier Revol, child psychiatrist and head of the Neuropsychiatry Department at the Pierre-Wertheimer Neurological Hospital in Lyon, told us in an interview[4] that "I preferred child psychiatry to adult psychiatry, where the possibilities of improving old pathologies are very limited. Early detection allows for early intervention, with appropriate care and often quite mild. The treatment is quickly effective and changes the future of the young patient completely. Not intervening often means allowing a sympatology to set in, the long-term consequences of which can be extreme, if not serious, at least complicated for the child".*

Is it a similar aspiration that drives you to devote so much energy and time to the care of the child's OSDB?

CG, MH-A, Y-SH, KL: We share Olivier Revol's view, which applies perfectly to the field of sleep. If there is no intervention on the factors that have an adverse impact on orofacial growth early in life with regular monitoring, obstructive sleep apnea (OSA) will occur and worsen with age. We would particularly like to draw your readers' attention to this important point.

We have shown that subtle abnormalities in oropharyngeal growth in infants and young children can contribute significantly to sleep disordered breathing and OSA later in life.

If left untreated, OSA affects children's quality of life, neurocognitive and academic performance, growth, behaviour, cardiovascular, carbohydrate and lipid systems.

Neurocognitive morbidity, which is reflected in hyperactivity, irritability, or even attention deficit disorder with or without hyperactivity (ADHD).

Agitation, lack of concentration or memory are often at the forefront and can be responsible for difficulties or delay in school. Indeed, repeated episodes of apnoea or hypopnoea are responsible for awakenings and micro-awakenings, leading to fragmentation and poor quality of sleep. Thus, it is important to look for OSA in any child with ADHD.

An improvement in neurocognitive disorders is observed after treatment of OSA in the vast majority of cases.

Cardiovascular morbidity, although less severe than in adults, is present with repeated episodes of airway obstruction which are associated with sympathetic hyperactivation with increased heart rate and blood pressure.

3.1. OSA and craniofacial growth

PA: *Harvold's work[71,178] has shown that dysfunctional nasal ventilation induces postural adjustments of the orofacial musculature and abnormalities in hard and soft tissue development. You have described how the interaction between abnormal stimulation of bone growth and the absence of nasal breathing, which is associated with secondary amplification of oral breathing, are responsible for abnormal development of the orofacial bony structures that support the upper airways, thereby increasing the risk of upper airway collapse during sleep[93,103].*

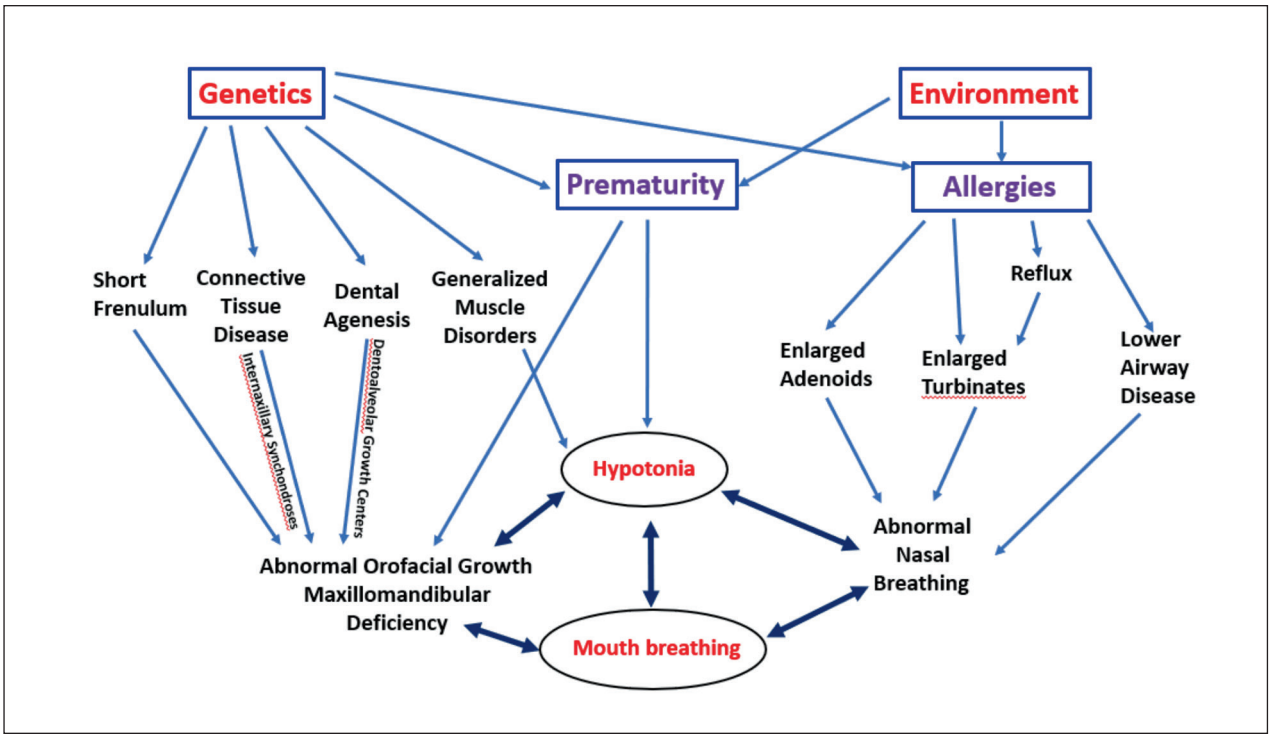


Figure 2
Abnormal development of the upper airways.

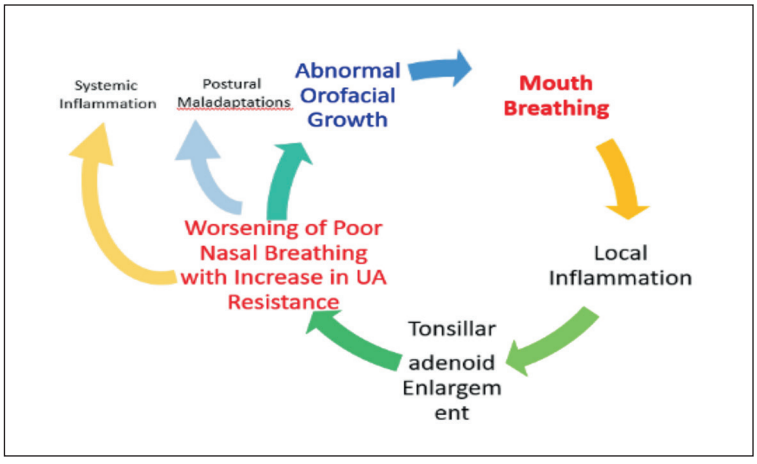


Figure 3
The vicious circle of SDB.

Before we discuss them in more detail in the following questions, can you remind us of the factors[39,40,44,48,51,78,84] that have a deleterious impact on the normal growth of the orofacial structures, and that contribute to the development of OSA in children and adults?

CG, MH-A, Y-SH, KL: Missing teeth, orofacial hypotonia, short lingual frenulum, are important factors as well as preterm birth. Our recent studies following a cohort of preterm Taiwanese children were published in BMC Pediatrics in 2014[84] and Sleep Medicine in 2019[82]. Sleep problems, neuro-developmental disorders and sleep-disordered breathing are more common in preterm infants than in term infants. We found that a very high percentage (80.6%) of preterm infants have an

AHI > 1/hour and 62.3% of preterm infants have a narrowing of the hard palate. These observations led us to propose a new concept, published in Sleep Medicine Reviews in 2018[44]: "From oral orofacial dysfunction to dysmorphism and the development of pediatric OSA". We have shown (Fig. 2) that after birth there is a continuous interaction between orofacial function and the growth of orofacial anatomical features. The dysfunctions identified to date as having a deleterious impact on orofacial development lead to sleep-disordered breathing through these disturbances in craniofacial growth.

Atypical craniofacial features, by increasing the risk of airway collapse, and oral breathing or poor nasal breathing disturbed by increased upper airway resistance, alter orofacial development.

Thus, a vicious circle is established with a continuous interaction between the factors leading to oral breathing and the oral breathing itself, which influences these factors (Fig. 3).

Therefore, the identification of risk factors, which ultimately lead to obstructive sleep apnoea, is essential. It can allow early recognition of these factors and the development of treatments to eliminate them early or at least reduce their impact, before they become more prevalent with age.

3.2. Ankyloglossia

PA: *The annual number of articles on ankylosing spondylitis has increased considerably in recent years[11]. Present in 4% to 11% of newborns, this anatomical and functional alteration of the lingual frenulum has deleterious effects on growth and craniofacial development[146,163] and may lead to breastfeeding difficulties[140] and maternal nipple pain[137]. You have shown that untreated ankyloglossia at birth is associated with OSAS in later life, and you advise that screening for the syndrome should be carried out when this anatomical abnormality is identified[51,85,184]. Can you enlighten our readers on this subject?*

CG, MH-A, Y-SH, KL: In one of our studies[184] we showed that restricted lingual mobility was associated with maxillary arch narrowing and soft palate lengthening. Our results suggest that variations in tongue mobility may affect maxillofacial development. A short, unoperated lingual frenulum at birth is associated with OSA in later life, and routine screening for the syndrome should indeed be performed when this anatomical abnormality is recognised[85].

Screening and correction of lingual frenulum shortness should be carried out early, if possible at birth, to optimize orofacial growth. Myofunctional therapy, combined with nasal breathing rehabilitation, is also necessary to restore normal sleep breathing in many children.

MH-A: A distinction must be made between the length of a frenulum and the type of anchorage of its insertions. A long lingual frenulum may nevertheless hinder lingual mobility due to its insertion levels and a short lingual frenulum hinders the proper functioning of the tongue by reducing its mobility.

As a reminder, Dahan[32] explained that the type of lesion observed depends on the height of the alveolar insertion of the lingual brake:
– high or cervical insertion is associated with a risk of mandibular incisor linguo-version;
– low or apical insertion is associated with a risk of mandibular incisor vestibulo-version;
– a sub-apical insertion is associated with a risk of mandibular recoil.

Ankyloglossia can prevent the posterior part of the back of the tongue from resting on the soft palate, thus compromising the physiological closure of the oropharynx necessary for nasal breathing and promoting the development of oral breathing. Ankyloglossia will cause functional disturbances directly related to postural changes as well as others generated by altered sensory signals. The earlier the intervention, the less growth will be affected.

Ventilation is oral and associated with a more anterior lingual posture, to clear the ABV. The presence of a too short brake will furthermore hinder the activity of the genioglossus, the "safety muscle". A ventilatory dysfunctional pattern has developed, altering the architecture of craniofacial growth.

KL: The concept behind the role of ankyloglossia in sleep is that ankyloglossia contributes

to a reduction in the mobility of the tongue and the muscular force it can apply to the palate, thus reducing the possibility of its development. Although this explanation of the involvement of a short lingual frenulum in the aetiopathogeny of airway collapse may seem logical to many, I would like to reiterate that there is currently no data to support it. We must be very careful when advocating surgery to release the lingual frenulum.

I believe that myofunctional therapy plays a role in improving the muscle strength of the tongue, but again we have too little data. In my practice, I ask patients to be assessed first by an orthophonist to check the strength of their tongue and the possible range of movement. I only agree to operate in cases where I feel I can improve the ankyloglossia and if the patient agrees to undergo myofunctional therapy.

PA: *Frenotomy is a low-risk procedure and is likely to be beneficial if the patient is carefully selected*[180]*. You have studied the effectiveness and reliability of instruments for assessing lingual mobility restrictions*[185]*. What were your findings? Which screening tool do you recommend for use and can you describe the scoring scale you proposed?*

CG, MH-A, Y-SH, KL: The objectives of this study were to evaluate the usefulness of existing instruments for the assessment of restricted tongue mobility, to describe normal and abnormal ranges of tongue mobility and to provide evidence for a reliable and effective measure of tongue mobility. We have shown that the maximum interincisal mouth opening depends on age and size and that the mouth opening with the tip of the tongue at the maxillary retroincisal papillae depends on the maximum interincisal mouth opening. Difference between the two previous measures, the deficit in the amplitude of tongue movements is the only independent measure of tongue mobility that is directly associated with restrictions in lingual function.

We proposed the use of the deficit in the amplitude of tongue movements as an initial screening tool to assess lingual mobility restrictions. Functional ankyloglossia can thus be defined and the effects of treatment objectively monitored using the proposed scoring scale: grade 1: tongue range of motion >80%; grade 2: tongue range of motion between 50-80%; grade 3: tongue range of motion <50%; grade 4: tongue range of motion <25%.

MH-A: The Kotlow technique appears to be the simplest to use. He recommends measuring the length of the frenulum from its insertion in the base of the tongue to its termination near the tip with the Boley gauge. According to the value found, he classifies the ankyloglossia from acceptable (greater than 16mm) to severe (less than 3mm).

PA: *If a frenotomy has not been performed in the infant, a lingual frenectomy may be performed at a later stage. Whatever the surgical modalities, it should be accompanied by lingual physiotherapy exercises to prevent recurrence, the rate of which has been estimated at 15%*[95]*. What exercises and what myofunctional therapy schedule do you recommend?*

CG, MH-A, Y-SH, KL: Recurrence has everything to do with how the operation is performed and whether the patient undergoes myofunctional therapy afterwards. Care must be taken to ensure that the surgical technique is not too aggressive and does not cause a lot of scarring.

3.3. Agenesis and dental extractions

PA: *Numerous studies*[8,121,132,142,169,170,176] *have reported alterations in craniofacial morphology observed in association with dental agenesis. These alterations could lead to decreased development and risk of upper airway collapse. You have studied the potential association between dental agenesis, early extraction of deficient teeth and the development of OSA in children*[39]*. Can you explain how you have shown that the absence of these teeth can lead to a reduction in nasal airflow?*

CG, MH-A, Y-SH, KL: To investigate the potential association between dental agenesis or early dental extractions and the presence of obstructive sleep apnoea (OSA), we examined clinical data, polysomnographic sleep studies and orthodontic imaging studies in children with dental agenesis or early extraction of permanent teeth in the previous five years and compared their results with those of children with normal dental development but adenoids and OSA symptoms. All children with agenesis or early extraction of permanent teeth, with at least two missing permanent teeth, had

complaints and clinical signs suggestive of OSA. In these children, advancing age was associated with the presence of a higher AHI.

We concluded that alveolar bone growth depends on the presence of teeth. Children with permanent teeth missing due to congenital agenesis or permanent tooth extraction had a smaller oral cavity, known to predispose to upper airway collapse during sleep, and had OSA diagnosed at a later age. We pointed out that due to the initial low-grade symptomatology, sleep-disordered breathing may go untreated for a prolonged period of time, with progressive worsening of symptoms over time.

PA: *Another of your publications[39] shows that the search for sleep-disordered breathing should be a constant concern in young children with agenesis. What are your recommendations in terms of family history, orthodontic treatment plan and goals?*

CG, MH-A, Y-SH, KL: The results of our studies show that the search for SRT should be an important concern for clinicians when faced with a young child with missing permanent teeth. Also, when SDB is present in a child, the history should address the family history of missing teeth and It is important to include the missing teeth (their location and number) in the clinical investigation.

We have often observed that children with congenital dental agenesis are hardly ever referred to a sleep centre immediately, and their parents are often reluctant to perform a sleep assessment that they do not perceive as necessary. As a result, referral to a sleep centre is often delayed and polysomnography is frequently only performed when sleep-related symptoms appear or are recognized.

Alteration of normal orofacial development may vary depending on the number of missing teeth, the age of the individual and the impact of the changes on the facial muscles. These changes may have a gradual impact on the width and stability of the upper airway during sleep and symptoms may only be noted by parents after a variable time interval.

Clinically, it is important for odontologists to be aware of the potential risk of developing OSA due to the absence of permanent teeth and to favour treatment approaches that avoid early extraction of permanent teeth.

PA: *In your video interview with Dr. Mike Milligan[73], you said about the use of dental avulsions in orthodontics: "we are very very against that" and you recalled that dental agenesis and early extraction of permanent teeth can lead to a reduction in nasal airflow. In an adolescent at risk of OSA, it does seem preferable to favour mandibular advancement orthognathic surgery rather than requesting avulsion of maxillary premolars to camouflage a class II malocclusion with mandibular retrognathia[6,75].*

In the case of macrodontia without associated sagittal or transverse anomalies, in adolescents or adults, do you think that the indication for extractions remains pertinal when their purpose is to avoid pushing the teeth out of the bone volumes and thus exposing the patient to an increased risk of gingival dehiscence, or to avoid imposing on the patient a maxillary disjunction associated with symphyseal distraction in order to avoid these extractions?

CG, M.-A, Y-SH, KL: Yes, after dental and skeletal diagnosis, the correction of tooth-arch disharmony (TAD) by macrodontia often involves a decision to extract permanent teeth. This is a therapeutic imperative in orthodontics when periodontal health and the durability of the treatment outcome are at stake.

We would like to point out that the need to intervene as early as possible in the case of OSDB implies that the treatment (maxillary disjunction, mandibular advancement orthosis or activator) should take place well before the age of the actual alignment treatment, including the correction of the DDA.

Yes, in the case of a class II malocclusion with mandibular retrognathia in the adolescent, if the therapeutic motivation is the management of a proven OSDB, it is clear that the surgical indication will be given. The worst case scenario would be a useless or even deleterious compromise of alignment therapy.

KL: Sometimes the extraction of permanent teeth is indeed necessary. However, one should

always try to expand rather than remove teeth. The problem is that most of the jaw expansion techniques used only push the teeth out by vestibulizing them, rather than actually expanding the jawbone. I have been able to develop an endoscopically assisted surgical expansion procedure in adults[114] as well as children to actually expand the naso-maxillary complex.

PA: *Thank you Kasey for this important clarification, which we will discuss in more detail below.*

3.4. Orofacial hypotonia

PA: *You have written that paediatric obstructive sleep apnoea in non-obese children is an orofacial growth disorder[40,78]. Can you remind us of the evidence that orofacial hypotonia[48] is a fundamental component in the development of anatomical abnormalities leading to abnormal breathing during sleep, and that there is a continuous interaction between orofacial muscle tone, maxillomandibular growth and the development of sleep-disordered breathing?*

CG, MH-A, Y-SH, KL: Figures 2 and 3 summarize the interrelationships between orofacial muscle tone, maxillomandibular growth and the development of sleep-disordered breathing. We have shown that in children preterm infants, certain generalized muscle disorders and factors such as short lingual frenulum and dental agenesis, which impact on orofacial growth and maxillomandibular impairment, will increase "hypotonia", the risk of a "hypoactive" condition.

The "mouth breathing" and the "narrow hard palate".

The development of the oral cavity begins around the second month of pregnancy. Fetal ultrasound has provided us with a great deal of knowledge and has shown fetal functions such as swallowing amniotic fluid, sucking, and certain reflexes involved in the development of the oral cavity. Other early life functions such as nasal breathing, sucking, swallowing, chewing and speaking are also related to orofacial development. Therefore, abnormalities in these functions increase the risk of abnormal development of the bony structures supporting the upper airway, leading to an increased risk of upper airway collapse during sleep.

The tongue plays a major role in the hypotony of the orofacial musculature. The early installation of the vicious circle of dysfunction/hypotonia will impact on growth and create the bed for future neuropathy.

PA: *For almost three decades[25], orofacial rehabilitation has been an integral part of orthodontic treatment, with the main objective of restoring optimal nasal ventilation[171,172]. At the 21st Congress of the European Sleep Research Society in September 2012 in Paris, two of your oral presentations[47,48] presented the results of a retrospective study on the efficacy of myofunctional rehabilitation in preventing relapse of OSA in children, and on hypotonia as a risk factor for recurrence of OSA at puberty. Can you report on your findings and the rehabilitation modalities that were implemented?*

CG, MH-A, Y-SH, KL: Limited data suggest that pubertal development may lead to recurrence of sleep-disordered breathing (SDB) despite prior curative adenotonsillectomy. Long-term myofunctional assessment in our retrospective cohort study[49] showed that after adenotonsillectomy, subjects who did not undergo orofacial myofunctional rehabilitation (OMR) had abnormal orofacial muscle tone when awake. They also had a recurrence of symptoms with a mean apnoea-hypopnoea index (AHI) of 5.3 ± 1.5 and a mean minimum oxygen saturation of 91 ± 1.8%, whereas the subjects who underwent OMR were symptom-free and had a normal functional status. Myofunctional rehabilitation consisted of strengthening the tongue and orofacial muscles by learning to reposition the muscles to the appropriate position and to breathe continuously through the nose.

3.5. Adolescent OSA

PA: *As early as 2007[46], you identified the symptomatology of adolescent OSA. Transition between childhood and adult OSA, adolescent OSA is predominantly type 291. Can you present the main pathophysiological, semiological and therapeutic characteristics of this condition?*

CG, MH-A, Y-SH, KL: Little research has been done on the specifics of OSA in adolescents. It is usually associated with overweight and obesity. It is indeed a type 2 OSA that adolescents suffer from, often without significant adenoidal-tonsillar hyper-

trophy. They have excessive daytime sleepiness and psychological disorders, and suffer from metabolic and cardiovascular complications.

Changes in sex hormone production, muscle hypertrophy, craniofacial skeletal maturation and obesity all contribute to the increased risk of developing OSA. The treatment of adolescent OSA is the same as for paediatric OSA, depending on the underlying causes.

3.6. Attention deficit disorder with or without hyperactivity

PA: *OSA may contribute to the symptomology of attention deficit hyperactivity disorder (ADHD) and treatment of OSA appears to have positive effects on ADHD symptoms[26,76,81,88,182]. You recommend that assessment of sleep disturbance be considered in all patients with ADHD, particularly before the start of medication[76]. What advice would you give to orthodontists who are in the front line of communicating this recommendation to their patients' families?*

CG, MH-A, Y-SH, KL: We have shown that OSA has a negative systemic impact. Not only does it cause cardiovascular dysfunction, but it also has clear effects on alertness, learning, memory, academic achievement, growth, abnormal behaviours suggestive of Attention Deficit Hyperactivity Disorder (ADHD), and mood disorders, such as depression and parasomnias, such as enuresis, sleepwalking and night terrors.

We also found[76] that inattention, neurocognitive function and learning problems improved after treatment of paediatric OSA. Therefore, if outpatients present with symptoms of inattention, hyperactivity, learning and emotional problems, daytime sleepiness and open-mouthed breathing during the day and snoring, enuresis and restless sleep at night, it is recommended to request a PSG and confirm the likely diagnosis of OSA.

The diagnosis of ADHD requires a consultation with a child psychiatrist and is only established following a very precise semiological approach. It is estimated that about 2% of ADHD has a ventilatory origin. Orthodontists have the privilege of seeing children at a very young age and it is useful to include some questions about sleep quality and behaviour in the initial consultation.

PA: *You advocate that OSA should be treated as early as possible to reduce the incidence of ADHD in children[81,181]. With this in mind, what do you think is the ideal age for a first consultation with an orthodontist?*

CG, MH-A, Y-SH, KL: We have suggested that the earlier OSDB is treated, the better the outcome. Treatment can start with orofacial myofunctional therapy implemented early in the baby's life. Usually, preschool children have a dental examination and if the dental surgeon or orthodontist observes the above symptoms, they should refer to a paediatric physician for polysomnography and treatment.

3.7. Snoring

PA: *In a 2004 commentary in Chest entitled "Does benign "primary snoring" ever exist in children? "[54] you stated that chronic snoring always has deleterious health consequences, including a possible increase in cardiovascular risk in adulthood[126], and that you had never observed a child with only primary snoring, provided the examination was appropriate[125]. Can you tell us what examinations should be carried out systematically in the case of a snoring child, including the examination of the craniofacial skeletal pattern?*

CG, MH-A, Y-SH, KL: From the point of view of preventive medicine, we believe that chronic snoring in children is not normal, and that snoring is a warning sign for their health. If children have open mouth breathing, adenoid face, mandibular retrognathia, narrow hard palate, nasal obstruction, open mandibular plane angle, increased facial height, we need to be alert. It should also be borne in mind that the analysis of the facial pattern of a snoring child is important but that this pattern does not always follow a precise type. It is the history that will guide our examination.

PA: *Together with Jacques Talmant, et al.[172], we have pointed out that structural changes secondary to the vibratory trauma caused by snoring can affect each component of the pharyngeal structures and contribute to the collapsibility of this segment of the airway. A prospective study[120] showed that in a group of 29 untreated men with sleepiness and snoring, the number of cases of OSA increased over 10 years from 4 to 13 ($p < 0.01$). Another[9] showed that patients with primary snoring or mild obstructive sleep apnoea showed a similar increase in the apnoea/hypopnoea index over time, which was*

mainly dependent on weight gain and, to a lesser extent, time. Have you observed any diagnostic and therapeutic evolution in the medical world, and particularly in orthodontists, with regard to snoring, which should never be considered a priori benign and should be systematically investigated?

CG, MH-A, Y-SH, KL: We believe that any flow limitation found on a sleep polygraph (SP) or PSG examination in children should be taken into account.

MH-A: In daily clinical practice, we play a screening role and refer the child or adolescent to the ENT specialist or paediatrician if necessary. Thanks to the French Society of Dental Sleep Medicine (SFMDS), awareness is evolving and inter-specialty links are improving. The double special issue of L'Orthodontie Française published in december 2019 and the multidisciplinary days co-organised by the Société Française d'Orthopédie Dento-Faciale (SFODF) and the SFMDS bear witness to this evolution.

PA: *Your recent prospective cohort study[128] analysed the relationship between snore sound energy (SSE) and the severity of obstructive sleep apnoea, as well as changes in SSE after adenotonsillectomy and predictors of surgical success in children with OSAS. Can you share your conclusions and perspectives with us?*

CG, MH-A, Y-SH, KL: We enrolled thirty-two children with OSA with apnea-hypopnea index ≥ 5 or apnea-hypopnea index ≥ 1.5 with comorbidities associated with OSA. All participants had undergone snore sound analysis, polysomnography and adenotonsillectomy. Snore acoustic energy and apnoea-hypopnoea index were assessed at baseline and six months after adenotonsillectomy. Surgical success was defined as a postoperative apnoea-hypopnoea index < 1.5. We showed that the snore sound energy (SSE) of 801-1000 Hz < 8.5 dB predicted significant surgical success. Our results suggest the potential usefulness of 801-1,000 Hz SSE as a potential biomarker for screening for severe OSA, predicting surgical success and evaluating therapeutic outcomes.

PA: *You examined the effects of cervical position[100] on obstructive sleep apnoea syndrome using a custom-designed cervical pillow to promote neck extension. What changes were observed according to the severity of OSA? As head posture has a marked effect on upper airway collapse, can our patients expect a therapeutic gain from the future development of such devices?*

CG, MH-A, Y-SH, KL: Our study on the effects of neck positioning on OSA using a neck pillow showed that subjects with mild OSA had a non-significant improvement in the severity of their snoring and a significant improvement in their respiratory disorder index with the neck pillow, while subjects with moderate OSA showed no improvement in these parameters. Subjects with severe OSA showed a slight improvement in some measures of their abnormal respiratory events over the experimental period. The usefulness of this positional treatment therefore appears to be limited at present.

PA: *You have shown the effectiveness of functional myotherapy on snoring in adults[17]. How is it prescribed for snoring children?*

Y-SH: In Taiwan, we have already conducted a few studies, two of which were published this year[29,83], showing, with PSG and cephalometric analysis of profile teleradiographs, the improvement of orofacial myofunctional therapy and passive myofunctional therapy (with the lingual stimulation ball brace developed by Michèle Hervy-Auboiron) in the treatment of paediatric OSA. Therefore, in our sleep centre, if non-obese children have snoring and do not have enlarged tonsils and adenoids, or after adenotonsillectomy, we will systematically implement orofacial myofunctional therapy or passive myofunctional therapy in them.

PA: *You have devoted several publications[60,147,159,160,161] to the surgical treatment of snoring. What is the current state of knowledge on this subject?*

KL: It is important to note that the treatments for snoring and OSA are essentially the same. I don't think there is such a thing as "simple snoring". Someone with "simple snoring" is a patient whose PSG has not been read and analyzed by someone with sufficient expertise to detect flow limitations, etc.

I always recommend non-invasive treatment first, such as a mandibular advancement orthosis, but only after informing patients of the risk of adverse effects on their occlusion.

The improvement in nasal breathing that can be seen is always important. I perform many endoscopically assisted surgical naso-maxillary expansions to treat snoring and OSA.

3.8. Restoration of nasal ventilation

PA: *You have shown that oral ventilation induces "disuse" of nasal breathing with changes in proprioception, posture and loss of use of the nose[103]. Chronic oral breathing, which is an important clinical marker of dysfunction of the orofacial musculature and may be associated with restricted palate growth[44,66,131], must be eliminated[65]. To restore nasal breathing during wakefulness and sleep, which you feel is the only valid criterion in the treatment of OSA[65], you recommend the use of myofunctional therapy[17,47,49,78,83] and passive myofunctional therapy with the Michèle Hervy-Auboiron device[77,103,119]. What do you think about the use of prefabricated myofunctional splints[105,106]?*

CG, MH-A, Y-SH, KL: Our studies have shown that chronic open mouth breathing is an important clinical marker of orofacial muscle dysfunction. Therefore, orofacial myofunctional therapy and passive myofacial therapy with the Michèle Hervy-Auboiron device are ways to achieve this goal of nasal breathing during wakefulness and sleep. Our studies have shown that such behavioural changes can be achieved by daily re-education exercises (orofacial myofunctional exercises) and by natural reflex action during sleep (Michèle Hervy-Auboiron device). It should be noted that the prerequisite for any re-education is the recovery of the vacuity of the VAS, with a possible indication of tonsillectomy and/or adenoidectomy upstream if necessary.

Assisting orofacial rehabilitation by wearing a splint requires, as with wearing a brace, informing patients of the risk of adverse effects on their occlusion. We await the publication of studies of sufficiently high methodological quality, with at least one control group, before expressing an opinion on the value of using these prefabricated devices for the treatment of paediatric obstructive sleep apnoea.

3.9. Therapeutic education

PA: *Sleep education programmes, especially in schools[12,94,141], are one way of informing people who suffer from sleep insufficiency. It should be noted that patient education, including therapeutic education[34], is similar to the approaches orthodontists use in daily clinical practice (awareness training[104], ortho-functional re-education[5], etc.) to develop adherence and optimize orofacial function in their patients, including ventilatory function[172]. What advice would you give to orthodontists to further help their patients achieve the compelling goal of restoring day and night nasal ventilation[65]?*

CG, MH-A, Y-SH, KL: Compliance of their patients can probably be improved by providing well-founded information on the health benefits of myofunctional rehabilitation and the risks involved if continuous nasal breathing during wakefulness and sleep is not restored.

3.10. Adenotonsillectomy

PA: *As the pathophysiological knowledge of OSA has evolved, so has the management of the infant, from tracheostomy, to continuous positive airway pressure, to adenotonsillectomy combined with orthodontic treatment and orofacial myofunctional rehabilitation[27]. Can you provide our readers with an overview of the key steps underlying this therapeutic evolution?*

CG, MH-A, Y-SH, KL: We have shown that removal of the tonsils and vegetations is not always followed by long-term therapeutic success[58] in paediatric OSAS. This recurrence called for a broader therapeutic arsenal, continuous positive airway pressure (CPAP) and maxillofacial surgery in the most severe cases. Then, the possibilities offered by orthodontics for the treatment of SRT opened a new therapeutic avenue. Rapid maxillary expansion, bimaxillary distraction and orofacial functional myotherapy were incorporated into the management of OSAS in children.

KL: Therapeutic advances involve many factors. Obviously, it's about reducing invasiveness and improving the effectiveness of therapeutic proposals. No one will advocate a tracheostomy today and we now understand that the use of CPAP in children often results in midface impairment. I think the indication for an adenotonsillectomy is

relevant (if the lymphoid tissue is enlarged) and naso-maxillary expansion with exercise can help most patients, but often the response is incomplete. I tell patients that there is no miracle cure and that we can only improve...

PA: *You[46,56,58,80] and other authors[101,156,162,167,174,175] have reported cases of recurrence of obstructive sleep apnoea in children operated on by adenotonsillectomy, despite the disappearance of symptoms and the normalisation of polygraphic tests observed after the operation. You have emphasised the need for a wider range of treatment than adenotonsillectomy, which you mentioned in your previous answer and which we would now like to discuss with you in more detail.*

CG, MH-A, Y-SH, KL: It will be a pleasure. The recurrence of paediatric OSA cases that we published was associated with changes in orofacial growth induced by oronasal dysfunction with the creation of negative feedback loops. The abnormal orofacial growth, induced by the ventilatory dysfunction, resulted in reduced development of the upper airways with an increased risk of collapse during sleep.

KL: I believe that endoscopically assisted surgical nasomaxillary expansion is superior to adenotonsillectomy in many children.

PA: *For adolescents with recurrence of symptoms after adenotonsillectomy, you have proposed the use of continuous positive airway pressure (CPAP)[59]. You have published extensively on CPAP[20,37,87,99,139,148,149,152] and you were the first[115] to explain the possible impact of the interface on the growth of the facial mass of the child[36,158] or even on the teeth of a 64 year old adult[145]? In addition to careful monitoring, what precautions can be taken to prevent this possible iatrogenic effect?*

CG, MH-A, Y-SH, KL: Continuous positive airway pressure (CPAP) for the treatment of obstructive sleep apnoea in children is a common treatment that can alter the normal growth of the facial skeleton due to the pressure exerted by the mask. This adverse effect calls for increased collaboration between sleep physicians and orthodontists to monitor mid-face growth during CPAP treatment.

MH-A: When CPAP is indispensable, temporarily or not, I have sometimes "cobbled together" a protraction mask on the face mask with support from a splint or an intraoral double-arch. The objective of this original association between the protraction mask and the face mask is to prevent the pressure exerted by the mask from maintaining or even aggravating a particularly deleterious retromaxillia.

PA: *For adolescents who become symptomatic again after adenotonsillectomy, you have shown that upper airway obstruction may be partially related to craniofacial risk factors[58,78]. You advocate that surgical treatment[56,153] should also aim to widen the airways and not just treat inflammation or infection of the lymphoid tissue. What types of interventions do you favour?*

CG, MH-A, Y-SH, KL: Absolutely, when airway enlargement is required, treatment of lymphoid tissue inflammation or infection alone may be insufficient to resolve residual symptoms after adenotonsillectomy. In such cases, further treatment, including collaboration with orthodontists to improve craniofacial risk factors, should be considered. In addition to allergy treatment, endoscopically assisted surgical naso-maxillary expansion may be offered.

PA: *The prevalence of allergic rhinitis in children with OSA or SRT is particularly high and children with SRT have a higher incidence of allergic rhinitis than those without SRT[22]. In addition, children with allergic rhinitis have an increased risk of persistent sleep-disordered breathing[92,102] after adenotonsillectomy. What specific follow-up do you recommend for them?*

CG, MH-A, Y-SH, KL: We recommend that children with allergic rhinitis undergo allergy treatment, such as desensitisation, whether or not they have had an adenotonsillectomy. In children with OSA who have had an adenotonsillectomy, the procedure should be followed by polysomnography and the children should do regular orofacial myofunctional exercises. In addition, oral breathing and craniofacial development, body weight and allergic rhinitis should be systematically monitored. If necessary, orthodontic treatment may be recommended.

PA: *You have published a long-term study[80] with systematic postoperative follow-up of adenotonsillectomies. You have shown that persistence and recurrence of obstructive sleep apnoea syndrome in children, with slow worsening of the apnoea-hypopnoea index (AHI), can frequently occur within three years, even in the context of a short-term postoperative benefit. Can you explain to our readers when and how you prescribe myofunctional rehabilitation[49] to help these patients achieve the necessary goal of restoring day and night nasal ventilation[65,103]?*

CG, MH-A, Y-SH, KL: In our study, we showed that adenotonsillectomy results in significant improvement in the apnea-hyporesia index, although usually with incomplete resolution, and we observed worsening over time in 68% of our cases. This high rate of recurrence requires routine orofacial myofunctional treatment before and after adenotonsillectomy. The exercise prescription varies from five minutes of exercise twice a day, four days a week for two months to ten minutes of exercise three to five times a day for three months.

3.11. Functional myotherapy

PA: *Functional myotherapy sessions are an aid not only to the treatment of sleep-disordered breathing[14,49,79] but also to the understanding of epigenetic phenomena in oro-naso-facial development, which play an important role in the genesis of sleep-disordered breathing in children[27]. What functional myotherapy modalities and exercises do you recommend?*

CG, MH-A, Y-SH, KL: Our latest study[50], which has just been accepted for publication by the journal Sleep, shows that the tongue is an essential organ with many receptors. It enables proprioception in the fetus and newborn and this sensory system is further refined in adolescence and adulthood. The tongue is the second largest sensory system in the body, after the tactile sensory system. The numerous receptors on its surface, especially the tactile mechanoreceptors, allow the recognition of shapes and surfaces of objects and play an important role in defending the tongue against biting, in eating, drinking and speaking. Therefore, it is essential that orofacial myofunctional rehabilitation includes lingual exercises such as:

1. Pull the tongue as far out of the mouth as possible.
2. With tongue out of mouth, touch right cheek.
3. With tongue out of mouth, touch left cheek.
4. With your tongue out of your mouth, try to touch the tip of your nose.
5. Place the tip of the tongue in the middle of the palate.
6. Place the tongue on the crowns of the upper teeth.
7. Stretch and place the tongue between the teeth and hold it there by squeezing gently.

These simple exercises are systematically prescribed to the small patients in our sleep centres.

PA: *In addition to the contribution of active orofacial myofunctional rehabilitation, you have also studied and shown the value of using passive myofunctional rehabilitation[30,77,119]. Can you share the results of your studies on this subject with our readers?*

CG, MH-A, Y-SH, KL: Yes, of course. In addition to the publications mentioned, we conducted a study[29], to be published at the end of the year, which aimed to evaluate the effects of one year of passive orofacial myofunctional rehabilitation (POMR) on craniofacial and airway morphology and quality of life in children with obstructive sleep apnea.

We showed that the apnoea-hypopnoea index (AHI), REM AHI, number of hypopnoeas and number of desaturations in the treatment group (with Michèle Hervy-Auboiron's oral tongue ball device) decreased significantly at PSG. Regarding airway morphology, the inter-group comparison showed that OPha-Ophp (distance between the anterior and posterior surfaces of the oropharynx) increased significantly in the treatment group. Regarding quality of life and clinical symptoms, the intergroup comparison showed statistically significant improvements in the treatment group (based on the OSA-18 questionnaire) for the following items: loud snoring, dysphagia, mood swings, discipline problems, waking difficulties, total score for the emotional distress section and total questionnaire score. We concluded that one year of OPMR using an oral device with a tongue ball improves AHI, nasal breathing during sleep, mandibular linear growth (Co-Gn and N-Me), airway morphology (OPha-Ophp) and clinical symptoms in children with OSA.

PA: *Michèle, can you describe the original device[30,77,119] that you created for these studies? What are the therapeutic concept, indications, wearing patterns and therapeutic effects?*

MH-A: The concept was born from a thought initiated by Alain Lautrou during our studies at the university diploma in occlusodontics: would it be possible to use a more functional orthosis to treat OSA?

The main objective of this custom-made one-piece mandibular advancement orthosis (patent number: EP 13753289.1; US14/420499) is to reduce external mechanical forces and increase muscle contribution, or even to rehabilitate.

Thus, Myonyx® would belong to the "tissue born appliances", i.e. the mucosal and non-dental supported thrusters. It is composed of a resin jaw tray fixed by two molar clasps. The mandible is free and only indentations guide the occlusion. This is calculated for an advance of 4-5 mm and a lowering of 3 mm. These values allow, according to Ahlgren and Bendéus[2], to remain within 20% of the muscle stretch or shortening coefficients.

A moving ball target is placed on a resin-embedded bracket located at the alveolar mucosa. The target is placed 2 mm from the lingual mucosa and approximately 3 mm below the gingival margin. When the patient opens his or her mouth, a reflex contraction of the lateral pterygoid occurs, called the Bass avoidance reflex. Pressure from the periodontal sensory receptors in contact with the target also stimulates the lingual propeller muscles. This is a survival mechanism designed to repel any object placed in the mouth; the tongue attempts to get rid of the foreign body.

The aim is to use targeted, appropriate and effective muscle recruitment. Our aim is to use the sensory properties of the tongue to enhance muscle recruitment and tone, while reducing stress on the teeth. While growth promotion is only possible in children, adults benefit from the minimal stress on their teeth that this device provides, in addition to a kind of passive myofunctional rehabilitation.

CG immediately joined the project and led the studies in adults in Europe and Canada and in children in Taiwan.

3.12. Maxillary retraction

PA: *Maxillary protraction devices can increase the size of the upper airway[33,134] and hopefully reduce the risk of OSAS in children with maxillary retrognathia[130]. Maxillary protraction with skeletal anchorage induces a greater skeletal effect than that achieved with facemask protraction[24,31]. You have studied the effects of using bone-anchored maxillary protraction to treat maxillary retrogression, malocclusion and obstructive sleep apnoea in children[151]. What were the findings?*

CG, MH-A, Y-SH, KL: Certainly, maxillary retrognathy creates an upper airway undersize problem that can be ameliorated in children with orthopaedic maxillary protraction, with dental or skeletal anchorage, or subsequent surgical maxillary advancement.

The results of these treatments have been most promising for pharyngeal airway enlargement. The objectives of our pilot study were to evaluate the use of bone-anchored maxillary protraction as a strategy for treating maxillary retrogression, class III malocclusion and obstructive sleep apnea in children.

Our preliminary results showed an improvement in apnoea-hypopnoea index (AHI) and OSA symptoms in the majority of children, as well as an improvement in respiratory and airway parameters with a highly significant change in the posteroanterior position of the maxilla and widening of the nasopharyngeal to oropharyngeal junction, compared to an untreated age- and sex-matched control group. The results depended on the age of treatment initiation and the patient's compliance with treatment.

3.13. Functional devices

PA: *Clinical studies show that functional device treatments increase the volume of the oropharyngeal airway and the anteroposterior position of the hyoid bone in growing patients with class II malocclusion[89,157,177,179]. They could thus reduce the potential risk of OSA in growing patients, as shown by two recent systematic reviews[86,183], although the latest Cochrane systematic review[23] could not conclude on the efficacy, or lack of it, of using functional devices for the treatment of obstructive sleep apnoea in children. What is your opinion?*

CG, MH-A, Y-SH, KL: Prospective studies on young growing patients are very difficult to implement because of possible ethical constraints. The research we have conducted in Taiwan is recognised as being methodologically rigorous. It shows that the treatment plan must be individualised on a case-by-case basis and that it is desirable to do everything possible to ensure that growth is expressed harmoniously and without constraints. The promise of functional therapy exists for OSAS in children. In the current state of knowledge, this is a real option. Primum non nocere.

3.14. Maxillary or bimaxillary expansion

PA: *You have studied the role of rapid maxillary expansion in the management of OSAS in children[16,143,144]. Can you give us the key points?*

KL: The key to naso-maxillary expansion is not expansion of the teeth or the socket! The goal is to expand the nasal airway. One should be cautious in thinking that the new expansion techniques with skeletal anchorage, such as MARPE (mini-screw-assisted rapid palatal expander) or DOME (Distraction osteogenesis maxillary expansion) are different, because they are not. The expansion model is the same as that of the traditional methods and all the data are available in the literature. The key to therapeutic effectiveness is to perform the expansion in the young subject. The average age of maxillary expansion in the meta-analysis you quoted[16] was 7.6 years.

PA: *Bucci, et al.[13] concluded their review of systematic reviews by stating that while rapid maxillary expansion allows for a significant increase in nasal cavity volume in the short and long term, maxillary expansion cannot currently be indicated when the sole objective is upper airway improvement and must therefore be supported by an orthodontic indication. Do you agree with their conclusion?*

KL: I strongly disagree, but I understand the reasoning behind their recommendation. You're trying to get an expansion of the nasal airway, but you're creating an over-expansion of the maxilla and disturbing the dental occlusion.

Therefore, I advocate pure or almost pure skeletal expansion to minimize dental changes. I have just published an article[114] in Sleep Medicine on this endoscopy-assisted surgical expansion technique for adults and hope to publish its application in children soon. This outpatient surgical procedure is designed to expand the maxilla to treat obstructive sleep apnoea. EASE (Endoscopically-assisted surgical expansion) is an outpatient procedure that improves nasal breathing and OSA by enlarging the nasal floor, not in a traditional V-shape, but of the same width from the anterior nasal spine

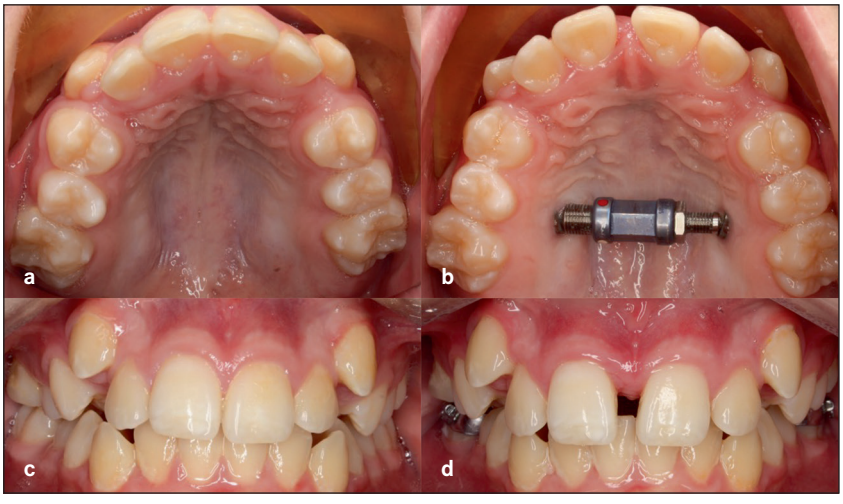


Figure 4

A child with OSA and maxillary dental crowding underwent endoscopically assisted naso-maxillary skeletal surgical expansion. Pre (a and c) and post (b and d) views (note the reduced size of the medial inter-incisal diastema showing the small impact of the skeletal expansion at the dento-alveolar level).

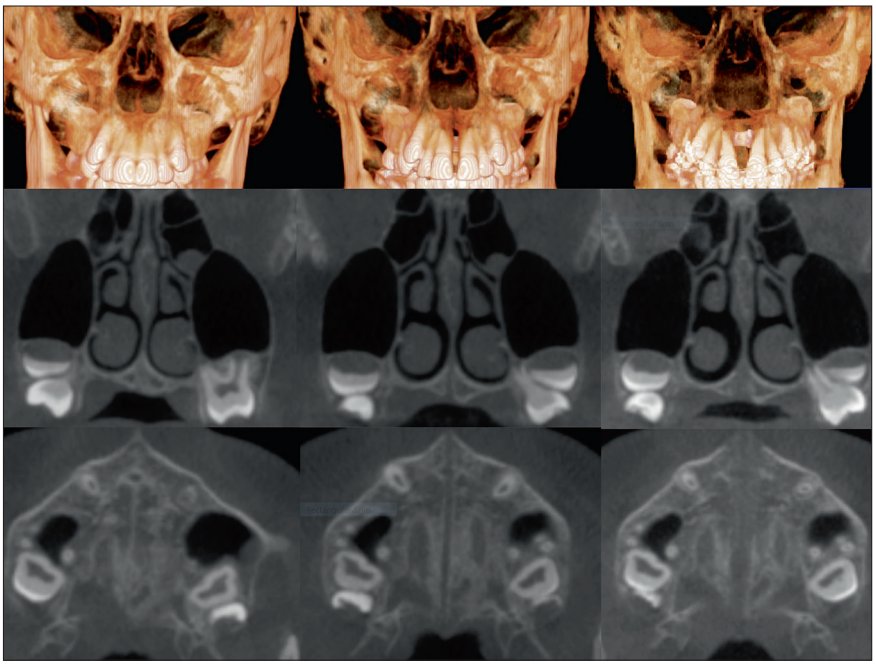


Figure 5

CBCT scans showing the progression of endoscopically assisted surgical expansion with complete separation of the median suture. Note the achievement of posterior expansion with complete separation of the suture between SNA and SNP, in contrast to typical fan expansion where anterior expansion may be excessive.

(ANS) to the posterior nasal spine (PNS) (Figs. 4 and 5). Compared to current surgical approaches for maxillary expansion, this new technique is considerably less invasive and allows airway enlargement with minimal complications.

PA: *You have shown that bimaxillary expansion, using rapid maxillary skeletal expansion and mandibular dentoalveolar expansion, improves the respiratory parameters of some children with OSA*[150]*. Can you tell us the conclusions of your study and its clinical perspectives?*

CG, MH-A, Y-SH, KL: Yes, the aim of our retrospective study was to evaluate the results of bimaxillary expansion, with rapid maxillary skeletal expansion and mandibular dentoalveolar expansion, as a treatment option for sleep-disordered breathing in children. Our results showed that the majority of children had improved sleep scores and symptoms after bimaxillary expansion. However, in the "mild OSA" group, patients with reduced mandibular plane angle or counterclockwise mandibular growth worsened with bimaxillary expansion, while patients with hourly mandibular growth showed greater improvement. In the severe OSA group, patients with mandibular retrognathia had less improvement in AHI.

PA: *Unlike the maxilla, non-surgical mandibular skeletal expansion is not possible. Only dentoalveolar expansion and the correction of a possible coronolinguoversion of the lateral sectors can be considered, within narrow limits, in order not to expose the patient to therapeutic recurrence*[72,122] *or gingival dehiscence. As a corollary, these therapeutic limits in the mandible require restricting the amount of maxillary expansion in order to preserve a satisfactory transverse occlusal setting.*

Symphyseal distraction[164] *allows surgically assisted skeletal mandibular expansion. The technique of osteogenic distraction applied to mandibular expansion has been proposed*[69,168] *for the treatment of OSDB. You were the first*[55] *to study the improvement in sleep-disordered breathing achieved by symphyseal distraction combined with maxillary disjunction or maxillary distraction. What were your findings and what are the indications for this therapeutic approach?*

KL: Christian and I did it many years ago, in 2004, and I don't do it now because the key to expansion

is really to widen the nose, which is achieved by my endoscopically assisted surgical naso-maxillary expansion technique[114].

3.15. Other surgical procedures

PA: *You have devoted many articles to the surgical treatment of OSA, of which I am only referencing the most recent ones*[15,18,19,21,108-114,116-118,123,124,133,154,155,173,186]. *What are the short- and long-term results and current indications of these various procedures?*

KL: Out of all the interventions you mentioned, I have selected the most effective ones and now I only do a few for children and adults. They give quite good results in most patients and, of course, patient selection is the key to therapeutic success.

I would mention, adenotonsillectomy in children if indicated, endoscopically assisted naso-maxillary expansion, nasal surgery and maxillomandibular advancement in adolescents if OSA is persistent.

In adults, I perform pharyngoplasty, if and only if the tonsils are large, nasal surgery (Fig. 6), endoscopy-assisted surgical naso-maxillary expansion and maxillo-mandibular advancement (Fig. 7).

4. Conclusion

PA: *In 2017, you wrote that "Many doors have been opened in a few years thanks to the study of OSA, but many questions still remain unanswered"*[27]. *We thank the four of you for holding these doors wide open to offer the readers of French Orthodontics a synthesis of some*

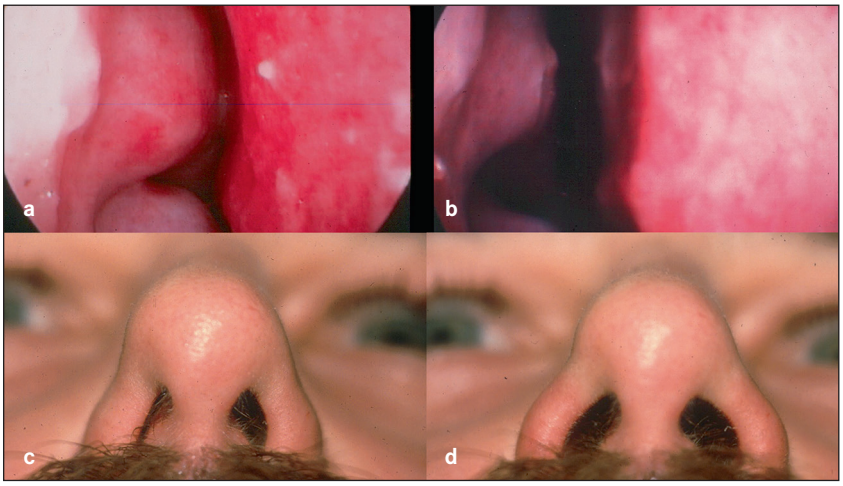


Figure 6
Nasal surgery and nasal valve repair. Before (a and c) and after (b and d) surgery.

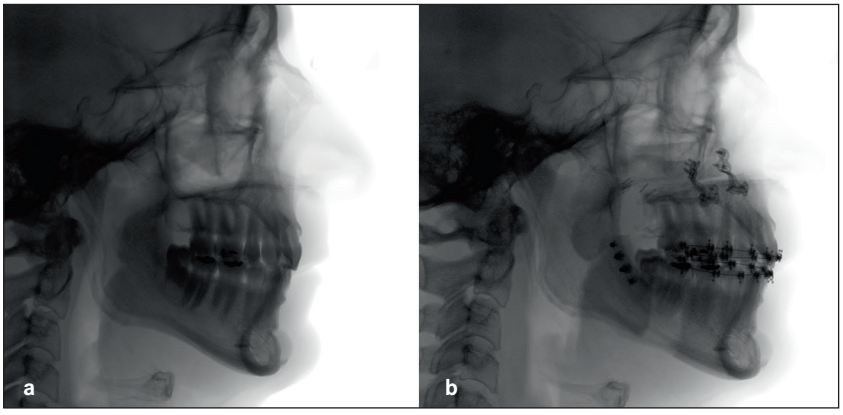


Figure 7
Profile teleradiographs, before (a) and after (b) maxillomandibular advancement surgery. Note the significant advancement while minimizing the use of titanium plates and screws, sometimes used in excess by some surgeons.

of the key elements of the relationship between sleep medicine and orthodontics.

CG, MH-A, Y-S.H, KL: We were pleased to be able to participate in this collegial interview, whose format allowed us to present the current state of the interrelationship between sleep medicine and orthodontics, while also giving us the opportunity to express the nuances of our individual views.

M.H-A: The main message to be retained from the work of CG is that everything is treated in childhood in terms of OSA. It is at this price that we can hope to avoid the irreversible adult neuropathy. It is clear that Jacques Talmant's work was a precursor.

Orthodontic and orthopaedic treatment is an essential part of the treatment of children's OSDB with a major functional focus. The world's most famous sleep therapist has not only given our speciality a noble status, but has also reaffirmed its mission.

Links of interest

The authors declare that they have no links of interest regarding the data published in this article.

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