

**EFFET DE LA PRESSION POSITIVE CONTINUE OU  
INTERMITTENTE ADMINISTRÉE PAR VOIE NASALE  
SUR LES DÉGLUTITIONS NON-NUTRITIVES CHEZ  
L'AGNEAU NOUVEAU-NÉ**

par

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## **LISTE DES ABRÉVIATIONS**

<b>DNN</b>	déglutition non-nutritive
<b>EEG</b>	électroencéphalogramme
<b>EOG</b>	électrooculogramme
<b>EVC</b>	éveil calme
<b>NA</b>	Noyau ambigu
<b>NFS</b>	Noyau du faisceau solitaire
<b>PPC</b>	pression positive continue
<b>SA</b>	sommeil agité (rapid eye movement sleep)
<b>SC</b>	sommeil calme (non rapid eye movement sleep)
<b>TA</b>	muscle thyroaryténo_dien
<b>VPPI</b>	ventilation à pression positive intermittente

## RÉSUMÉ

Alors que les problèmes respiratoires et de déglutitions sont fréquemment rencontrés en période néonatale, l'interaction entre ces deux phénomènes demeure encore très peu documentée. Ceci est particulièrement vrai dans des conditions où un support ventilatoire nasal en pression positive continue (PPC) ou en pression positive intermittente (VPPI) est employé chez les nouveau-nés. Alors que des résultats obtenus chez l'adulte démontrent qu'une PPC nasale inhibe les déglutitions induites par l'eau (Nishino T, 1989), les effets de la PPC ou VPPI nasale sur les déglutitions sont totalement inconnus chez le nouveau-né. Ainsi, les objectifs de ce projet sont de vérifier 1) si une PPC nasale inhibe les déglutitions non-nutritives (DNN) ; 2) l'effet de la VPPI sur les DNN ; 3) l'effet de la PPC et de la VPPI nasale sur la coordination respiration-DNN et 4) l'effet des stades de conscience.

**Méthodes.** Douze agneaux nés à terme ont été instrumentés chirurgicalement à 48h de vie afin de recueillir les DNN, les mouvements respiratoires, l'activité électrique du diaphragme, les stades de conscience, l'oxygénation artérielle (oxymétrie pulsée) et la fréquence cardiaque. Trois enregistrements polysomnographiques de 4 à 6h ont été effectués sans sédation entre 4 et 6 jours de vie, en randomisant les modes ventilatoires étudiés [absence de support ventilatoire (contrôle), PPC 6 cm H<sub>2</sub>O et VPPI 10/4 cm H<sub>2</sub>O]. Tous les enregistrements ont été effectués grâce à un système de télémétrie conçu et développé dans notre laboratoire.

**Résultats.** Les résultats montrent que globalement, la PPC diminue significativement la fréquence des DNN, plus spécifiquement les DNN isolées en sommeil calme et les DNN en bouffées en sommeil agité. En comparaison, les effets de la VPPI sont plus variables, avec une diminution significative de la fréquence des DNN à l'éveil seulement, et une augmentation significative de la fréquence des DNN isolées en sommeil agité. Finalement, ni la PPC ni la VPPI n'altère la coordination entre les DNN et les phases du cycle respiratoire.

**Conclusion.** La PPC 6 cm H<sub>2</sub>O nasale inhibe les DNN chez l'agneau nouveau-né. La pertinence clinique de cette nouvelle découverte est reliée à l'importance des DNN en période néonatale pour la clairance des sécrétions et du contenu gastrique qui reflue fréquemment dans le pharynx. De plus, les modifications des DNN, par l'administration prolongée d'une PPC nasale en période néonatale, pourraient avoir un impact sur la maturation de la fonction de déglutition, dû à la plasticité du cerveau du nouveau-né.

**Mots-clés :** Déglutition non-nutritive, support ventilatoire nasal, stades de conscience, coordination respiration-déglutition

## **INTRODUCTION**

### **Déglutition**

Par définition une déglutition est un acte complexe au cours duquel sont mis en jeu, selon une séquence prédéterminée, un grand nombre de muscles situés au niveau de la cavité buccale, du pharynx, du larynx et de l'œsophage (Car E, 1998).

### **Caractérisation du phénomène**

La fonction essentielle de la déglutition est le transport actif des aliments solides et liquides de la bouche à l'estomac. Elle sert également à protéger les voies respiratoires inférieures d'une pénétration de matières ingérées, régurgitées ou normalement sécrétées (salive). Ainsi, il est primordial de distinguer la déglutition nutritive de la déglutition non-nutritive (DNN). D'une part, la déglutition nutritive s'effectue au cours des périodes d'alimentation et sert principalement à la propulsion du bol alimentaire vers l'estomac. Ce type de déglutition se caractérise par des mouvements répétitifs. D'autre part, la déglutition non-nutritive, qui s'effectue en dehors des périodes d'alimentation, sert principalement à la clairance des sécrétions salivaires oro-pharyngées et se caractérise plutôt par des mouvements isolés.

## **Phases de la déglutition**

Le déroulement de la déglutition se divise en trois phases : 1) buccale, 2) pharyngée et 3) oesophagienne.

Premièrement, la phase buccale est définie comme étant une phase volontaire, complexe et très rapide (durée variable  $\approx$  1 seconde). Cette phase assure la propulsion du bol alimentaire d'avant en arrière à travers la cavité buccale. Elle est précédée par une préparation du bol alimentaire qui consiste en la préhension, la mastication et l'insalivation des aliments (ce n'est pas la déglutition proprement dite). Trois paires de nerfs crâniens sont impliquées dans l'élaboration de cette phase soit : le nerf trijumeau (branche maxillaire; V), glosso-pharyngien (IX) et le vague (nerf laryngé supérieur; X). Durant cette phase, la contraction des muscles des lèvres et des joues (muscle orbiculaire de la bouche et buccinateur) est primordiale afin d'empêcher les aliments solides et liquides de s'échapper par la cavité orale.

Deuxièmement, la phase pharyngée, sous contrôle involontaire (réponse réflexe), sert à propulser le bol ainsi qu'à protéger et fermer les orifices où le bol ne doit pas pénétrer (cavité nasale et cavité laryngée). La propulsion à ce niveau est assurée par la contraction des constricteurs du pharynx (constricteur supérieur, moyen et inférieur). La communication avec le nasopharynx est obturée grâce à la contraction des muscles du voile du palais. Simultanément, le larynx est activement fermé par la contraction des muscles suprahyoïdiens (mylohyoïdien et géniohyoïdien) et thyrohyoïdien, qui tire le bloc os hyoïde-larynx vers le haut et en avant sous la base de la langue, tandis que l'épiglotte se



bascule et que la musculature interne du larynx se contracte (muscles thyroaryténoïdien, interaryténoïdien, cricoaryténoïdien latéral et cricothyroïdien). Cette phase dure environ 1 seconde et s'accompagne toujours d'un arrêt respiratoire durant 600 ms à 1s. Les principales paires de nerfs crâniens impliquées dans cette phase sont le X et XII (hypoglosse).

Finalement, la phase oesophagienne, également sous contrôle involontaire, est très simple et d'une durée de plus de 10 secondes. Cette phase débute toujours par la relaxation et l'ouverture du sphincter supérieur de l'œsophage (muscle crico-pharyngien) et se poursuit par une contraction péristaltique du muscle oesophagien. Elle se termine par la relaxation et l'ouverture du sphincter inférieur de l'œsophage (cardia) et par passage du bol dans l'estomac (sous l'influence du vague).

### **Séquence motrice stéréotypée**

La déglutition est une séquence motrice stéréotypée impliquant la contraction de plus de 25 paires de muscles, qui englobe les muscles de la mâchoire et muscles périoraux, muscles sous-mandibulaires / suprahyoïdiens, muscles de la langue, muscles pharyngés et laryngés et muscle crico-pharyngien du sphincter supérieur de l'œsophage (Miller A, 1982; Jean A, 2001) (Figure 1). Il existe ainsi une coordination très fine entre les divers muscles impliqués dans ce phénomène. C'est l'un des réflexes les plus complexe du style tout ou rien.

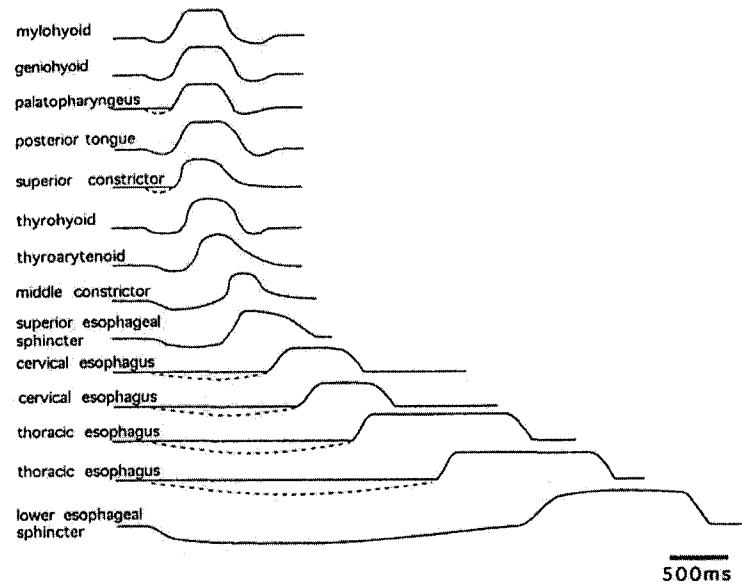


Figure 1 : Contraction successive des divers muscles impliqués dans la séquence motrice stéréotypée d'une déglutition (Jean A, 2001)

### Organisation neuronale

Le centre déglutiteur, localisé dans le bulbe rachidien et la protubérance du tronc cérébral, est constitué de neurones associés à la déglutition. Il déclenche et contrôle la séquence motrice en fonction des informations qu'il reçoit de la périphérie (récepteurs sensoriels) et/ou du cortex cérébral. Ce centre est subdivisé en trois étages : 1) étage afférent ou sensitif; 2) étage efférent ou moteur; 3) étage organisateur (Car E, 1998).

L'étage afférent est impliqué dans l'initiation et la facilitation du réflexe de déglutition. Il est composé de fibres nerveuses afférentes (V, IX, X) qui convergent et se terminent dans le noyau du faisceau solitaire (NFS).

L'étage efférent contient l'ensemble des motoneurones mis en jeu lors d'une déglutition. Ces motoneurones assurent l'innervation motrice des muscles (Figure 1) impliqués dans la déglutition. Les efférences sont acheminées vers les muscles via les nerfs crâniens facial (VII), glosso-pharyngien (IX), vague (X) et hypoglosse (XII).

Finalement, l'étage organisateur est constitué d'un réseau d'interneurones qui assurent la programmation de l'acte et la distribution successive de l'excitation aux divers groupes de motoneurones concernés. Ainsi, deux amas d'interneurones, présentant une activité étroitement corrélée avec la déglutition, ont été localisés dans le bulbe rachidien. Premièrement, un amas dorsal localisé dans le NFS et la substance réticulée sous-jacente. Ces interneurones reçoivent des afférences en provenance de la périphérie et/ou du cortex cérébral. Ils sont impliqués dans l'élaboration du programme de déglutition et dans le déclenchement de l'acte. Deuxièmement, un amas ventral localisé dans la substance réticulée autour du noyau ambigu (NA). Ces interneurones, activés par l'amas dorsal, distribuent le programme de déglutition aux différents groupes de motoneurones.

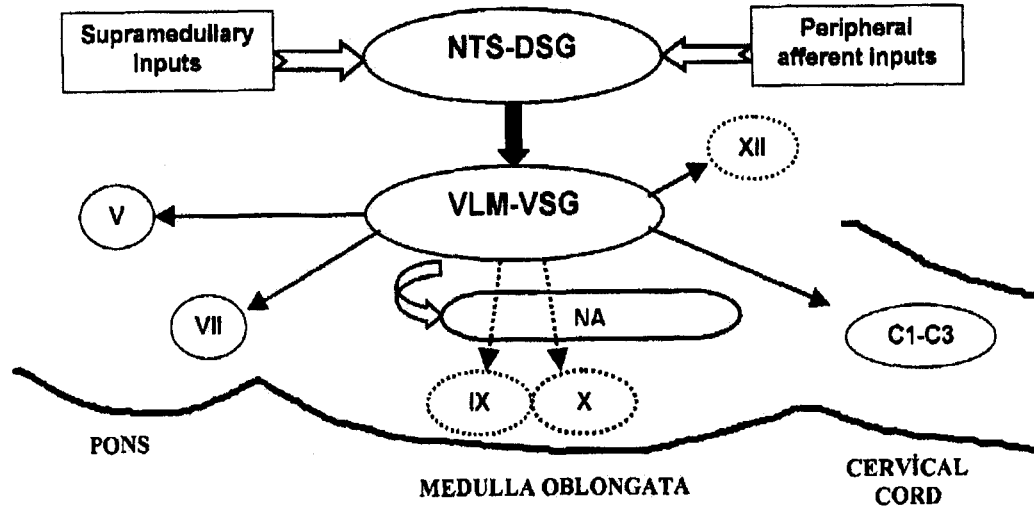


Figure 2 : Organisation neuronale du centre de déglutition (Ertekin C, 2003)  
 DSG : Dorsal swallowing group (amas dorsal) ; VSG : ventral swallowing group (amas ventral)

### Coordination déglutition et respiration

La respiration et la déglutition sont deux phénomènes physiologiques qui ne peuvent s'effectuer simultanément, puisqu'ils partagent un passage commun (pharynx). En effet, ces deux phénomènes doivent être parfaitement coordonnés afin d'assurer une ventilation adéquate sans induire d'aspiration pulmonaire et d'apnées prolongées. Ainsi, lorsqu'un ordre de déglutition part du centre déglutiteur bulbaire vers les effecteurs, des influx inhibiteurs partent sur les centres respiratoires pour inhiber la commande inspiratoire centrale. Dans cet ordre d'idées, il est intéressant de souligner la juxtaposition anatomique des centres déglutiteur et respiratoires, tant au niveau du NFS que du NA.

Les déglutitions ont été classées en fonction de leur survenue à l'intérieur du cycle respiratoire. Elles ont été décrites en fonction de la phase respiratoire qui précède et suit la déglutition. Quatre types de déglutition ont été décrites (Reix P, 2003) : déglutition de type ee (précédée et suivie par une expiration), déglutition de type ei (située à la transition entre une expiration et une inspiration), déglutition de type ie (située à la transition entre une inspiration et une expiration) et déglutition de type ii (précédée et suivie par une inspiration) (figure 3).

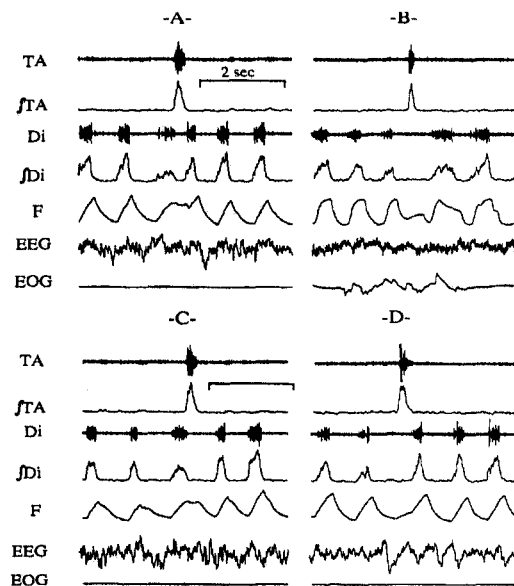


Figure 3 : Relation entre respiration et déglutitions non-nutritives (Reix P, 2003)  
 Chaque tracé montre de haut en bas : TA : EMG brut du muscle thyroaryténoïdien;  $\int$ TA : EMG intégré du TA; Di : EMG brut du diaphragme;  $\int$ Di : EMG intégré du Di; F : flux nasal (inspiration vers le haut); EEG : électroencéphalogramme; EOG : électrooculogramme.  
 A) déglutition de type ii B) déglutition de type ee C) déglutition de type ie D) déglutition de type ei.

## **Support ventilatoire nasal**

L'administration nasale d'une pression positive est non-invasive et ne nécessite pas d'intubation endotrachéale. L'administration s'effectue donc via une canule nasale (simple ou double) ou via un masque nasal. Ce support ventilatoire est de plus en plus favorisé et utilisé puisqu'il permet d'éviter les nombreuses complications reliées à l'intubation endotrachéale. En effet, l'utilisation prolongée d'une ventilation mécanique *via* un tube endotrachéal, peut engendrer de nombreuses complications telles que traumatismes laryngés (ex : luxation aryténoïdienne), sténose sous-glottique, infections des voies respiratoires sous-glottiques, hémorragies d'origine trachéale et altération de la fonction muco-ciliaire trachéo-bronchique (Northway WH, 1967 ; Charafeddine L, 1999 ; Krauss AN, 1975 ; Albert DM, 1990).

L'administration d'un support ventilatoire nasal apporte de nombreux bénéfices cliniques. En effet, le support ventilatoire nasal est de plus en plus utilisé en période néonatale dans le traitement des apnées des prématurés (Davis P, 1999 ; Linch CH, 1998), des syndromes de détresse respiratoire chez les prématurés (maladie des membranes hyalines) (Tooley J, 2003 ; Polin Ra, 2002; Verder H, 1999) et pour le sevrage de la ventilation mécanique endotrachéale (De Paoli AG, 2003 ; Espagne S, 2002). De plus, l'administration d'une pression positive continue nasale (PPC) associée à l'instillation préventive très précoce de surfactant est utilisée comme traitement primaire de la maladie

des membranes hyalines, pour diminuer l'incidence et la gravité de cette maladie (Storme L, 1999).

L'administration d'un support ventilatoire nasal peut s'effectuer selon plusieurs modalités. En période néonatale, l'administration d'une pression positive continue (PPC) ou d'une ventilation à pression positive intermittente (VPPI) est couramment utilisée. Par définition, le mode PPC est simplement le maintien artificiel d'une pression dans les voies respiratoires à un niveau supra-atmosphérique constant durant tout le cycle respiratoire ; le patient génère en totalité les efforts respiratoires nécessaires pour assurer sa ventilation pulmonaire (Figure 4). Au contraire, la VPPI prend en charge une partie du travail respiratoire du patient, selon différentes modalités disponibles. Dans le mode aide inspiratoire (encore appelé pression de support), la pression positive délivrée par le ventilateur à l'inspiration est déclenchée par l'effort du patient. Selon le ventilateur mécanique utilisé, le signal traduisant l'effort inspiratoire est un signal de débit inspiratoire ou de pression « négative » (par rapport au niveau de pression de fin d'expiration) mesuré à l'entrée des voies aériennes. La pression inspiratoire positive pré réglée est délivrée par le ventilateur tant que le patient assure un effort inspiratoire. Le début de l'expiration par le patient (signal de débit expiratoire ou de pression positive à l'entrée des voies aériennes) entraîne l'arrêt de la pression positive inspiratoire délivrée par le ventilateur. L'expiration est alors caractérisée par le retour des pressions dans les voies aériennes à un niveau expiratoire préétabli (le plus souvent un certain niveau de pression positive à la fin de l'expiration) (Figure 5). Ces deux supports

ventilatoires (PPC et VPPI) permettent de maintenir les voies aériennes supérieures ouvertes lorsqu'elles ont tendance à se collaber (apnées obstructives), favorisent le recrutement des zones atelectasiées (Millar D, 2004), augmentent le volume de fin d'expiration au-dessus de la capacité résiduelle fonctionnelle, la  $PO_2$  alvéolaire et la diffusion alvéolo-capillaire. De plus, la VPPI retarde la survenue de la fatigue des muscles ventilatoires, en prenant en charge une partie du travail inspiratoire.

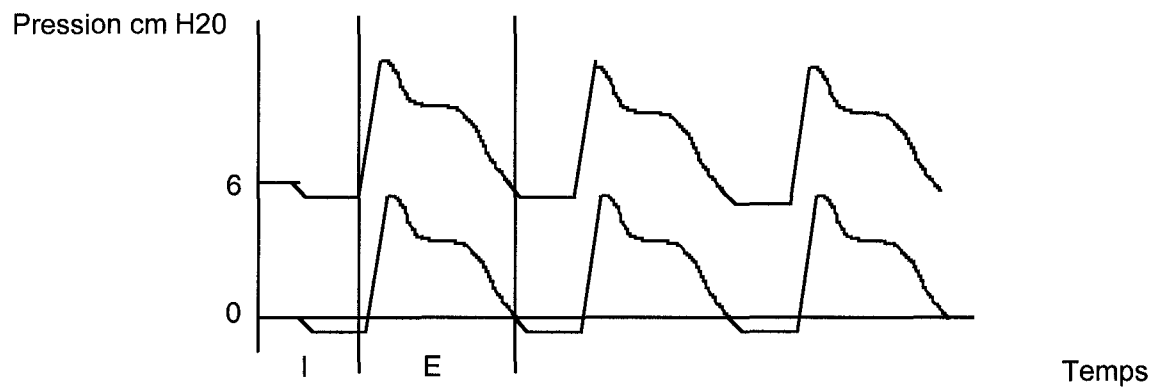


Figure 4 : Illustration schématique de l'administration d'une PPC. I = phase inspiratoire; E = phase expiratoire; ligne noire = respiration spontanée; ligne grise = respiration spontanée sous une PPC de 6 cm H<sub>2</sub>O nasale.



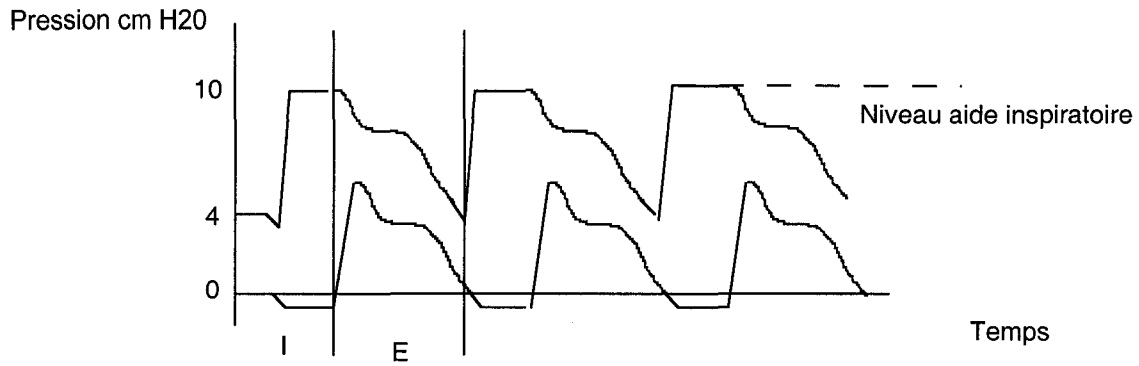


Figure 5 : Illustration schématique de l'administration d'une VPPI. I = phase inspiratoire; E = phase expiratoire; ligne noire = respiration spontanée; ligne grise = respiration spontanée sous une VPPI nasale de 10/4 cm H<sub>2</sub>O (10 cm H<sub>2</sub>O de pression inspiratoire et 4 cm H<sub>2</sub>O de pression expiratoire).

### **Contexte de l'étude**

Les troubles de déglutitions nutritives sont, avec les problèmes respiratoires, les problèmes les plus fréquemment rencontrés en néonatalogie. Ainsi, un nouveau-né prématuré ne peut pas boire avant l'âge de 35 semaines d'âge post-conceptionnel. De nombreuses études se sont attachées à la caractérisation de l'immaturité de la déglutition nutritive chez le nouveau-né, et à sa maturation postnatale (Mathew OP, 2003). Cependant, très peu d'études se sont intéressées, malgré leur grande importance, aux DNN, responsables de la clairance de la salive, des sécrétions d'origine respiratoire (nasales, trachéo-bronchiques) et de liquide reflué de l'estomac. Ces DNN ont aussi une importance cruciale chez le nouveau-né, puisqu'à cet âge le sphincter inférieur

de l'œsophage est immature, et est ainsi responsable de reflux gastro-pharyngés chez virtuellement tous les nouveau-nés. Ces reflux pharyngés les exposent à des apnées, des bradycardies et des désaturations de l'oxyhémoglobine *via* les chémoréflexes laryngés et/ou des aspirations trachéales. Les chémoréflexes laryngés sont impliqués dans les apnées du nouveau-né et du nourrisson, dans les malaises graves du nourrisson, et dans certains cas de syndrome de mort subite du nourrisson (Page M, 2000 ; Thach BT, 2001 ; Wetmore RF, 1993).

Nous avons récemment étudié dans notre laboratoire la fréquence des DNN, la coordination des DNN avec les différentes phases du cycle respiratoire et les rapports DNN-apnées spontanées au cours des différents stades de conscience chez l'agneau nouveau-né. L'effet de la prématurité a aussi été étudié. Les résultats de ces études ont été rapportés dans deux articles récents (Reix P, 2003 ; Reix P, 2004) et constituent les premiers résultats significatifs à cette période. Par contre, dans les unités de soins intensifs néonataux plusieurs conditions (ex. tachypnée, hypoxie, hypercapnie) ou interventions thérapeutiques (ex. application d'une pression positive) peuvent en théorie interférer avec les DNN et leur coordination avec les phases du cycle respiratoire. Une étude antérieure (Nishino T, 1989) effectuée sur des adultes conscients, et qui a démontré que l'application nasale d'une PPC inhibe les déglutitions induites par l'eau, est d'ailleurs bien intéressante à cet égard. Ainsi, notre étude s'intéresse à l'effet potentiel de l'application d'une PPC et VPPI sur les DNN en période néonatale. En effet, la question posée maintenant dans ce travail est : quel est l'effet d'un support ventilatoire nasal (fréquemment utilisé chez le nouveau-né)

sur la fréquence des DNN et leur coordination fine avec le cycle respiratoire. Dans ce premier travail sur le sujet, l'effet d'une exposition aiguë (quelques heures seulement) sera étudié.

**ARTICLE**

**Effect of nasal continuous or intermittent positive airway  
pressure on non-nutritive swallowing in the newborn lamb**

**Nathalie Samson**, Marie St-Hilaire, Elise Nsegbe, Philippe Reix, François Moreau-Bussière, Jean-Paul Praud. Soumis à *Journal of Applied Physiology*

**Effect of nasal continuous or intermittent positive airway pressure on non-nutritive swallowing in the newborn lamb**

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## **ABSTRACT**

The present study was aimed at investigating the effects of nasal continuous positive airway pressure (nCPAP, 6 cm H<sub>2</sub>O) or intermittent positive pressure ventilation (nIPPV, 10/4 cm H<sub>2</sub>O) on non-nutritive swallowing (NNS) and on the coordination between NNS and phases of the respiratory cycle, while taking into account the potential effects of states of alertness. Twelve full-term lambs were chronically instrumented at 48h after birth for polysomnographic recordings, including NNS, diaphragm electromyographic activity, respiratory movements, pulse oximetry and states of alertness. Studies in control conditions, with nCPAP and nIPPV were performed in random order in non sedated lambs at 4, 5 and 6 days of life. Results demonstrate that nCPAP significantly decreased overall NNS frequency, more specifically isolated NNS during quiet sleep and bursts of NNS in active sleep. In comparison, the effects of nIPPV on NNS frequency were more variable, with an inhibition of NNS only in wakefulness, and an increase in isolated NNS frequency in active sleep. In addition, neither nCPAP nor nIPPV disrupted the coordination between non-nutritive swallowing and phases of the respiratory cycle. In conclusion, nCPAP inhibits NNS occurrence in newborn lambs. Clinical relevance of this novel finding is related to the importance of NNS for clearing the upper airways from secretions and gastric content frequently regurgitated in the neonatal period.

**Keywords:** Control of breathing; sleep; radiotelemetry; upper airways; larynx

## **INTRODUCTION**

While swallowing and respiratory problems are among the most frequent disorders encountered in neonates (1, 6) the interrelationships between both of these functions are not completely known. This is especially true for non-nutritive swallowing (NNS), which fulfills the important function of clearing upper airways from secretions and liquids refluxed from the stomach. The latter is particularly relevant to the neonatal period, when immaturity of the lower esophageal sphincter is responsible for gastroesophageal reflux in virtually all infants, exposing them to apneas, bradycardias and oxyhemoglobin desaturation *via* the laryngeal chemoreflexes and/or tracheal aspiration. Recent studies in infants (4) and in full-term and preterm lambs (16, 18) have provided new information on NNS in basal conditions, including the effects of states of alertness and the links with apneas. However, conditions in the neonatal intensive care units are frequently far from “basal”, and many conditions (*e.g.*, tachypnea) or therapeutic interventions (*e.g.*, nasal application of airway positive pressure) may interfere with NNS and its coordination with breathing. The present study focuses on the potential effects of nasal continuous positive airway pressure (CPAP) and intermittent positive pressure ventilation (IPPV) on NNS in the neonatal period, for two reasons. First, previous results in awake human adults suggest that nasal CPAP inhibits water-induced swallowing (13). To our knowledge, these are the only available results on the effects of nasal application of positive airway pressure on NNS in the medical literature. Secondly, nasal CPAP (nCPAP) and

nasal IPPV (nIPPV) are increasingly being used in newborns for treating apneas of prematurity (2,11) and respiratory distress syndrome (15, 22, 23) as well as for reducing the rate of extubation failure following endotracheal mechanical ventilation (3, 5). The aim of the present study conducted in newborn lambs was therefore to 1) test the hypothesis that nasal CPAP and IPPV decreases NNS frequency; 2) examine whether nasal CPAP and/or IPPV influences the coordination between NNS and phases of the respiratory cycle; and 3) assess the potential effects of states of alertness.



## **MATERIAL AND METHODS**

### **Animals**

A total of 12 mixed-bred lambs were involved in the study. All lambs were born at term by spontaneous vaginal delivery at our local provider's farm. The protocol of the study was approved by the ethics committee for animal care and experimentation of the University of Sherbrooke.

### **Surgical preparation**

Aseptic surgery was performed on the second day of life under general anesthesia (2% isoflurane-30% N<sub>2</sub>O-68% O<sub>2</sub>). Anesthesia was preceded by an intramuscular injection of atropine sulfate (0,1 mg/kg) and ketamine (10mg/kg). Antibiotics (5 mg/kg gentamicin and 50 mg/kg ampicillin) were administered intramuscularly before surgery and daily until the end of the experiments. One dose of ketoprofen (3 mg/kg intramuscularly) was systematically given immediately after induction of the anesthesia for analgesia and repeated if needed the next day. Chronic instrumentation included placement of bipolar enameled chrome wire electrodes (diameter 0.1 mm) in both thyroarytenoid (TA, a glottal constrictor) and diaphragm muscles for electromyographic (EMG) activity recording (7). Custom-made electrodes for electroencephalogram (EEG) and electrocardiogram (ECG) were placed as previously described (19). Two platinum needle electrodes (F-E2, Grass instrument Company, Quincy, MA) were placed into the outer lower region, and the inner upper region of the right eye

socket for electrooculogram (EOG) recording. Finally, a catheter was introduced in the artery of the forepaw of each lamb, to collect arterial blood samples for analyses of pH, PaO<sub>2</sub>, PaCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> concentration. This catheter was left in place for the entire duration of the study and flushed daily with heparin solution. Leads from each electrode were subcutaneously tunnelled to exit on the back of the lambs. Correct electrode positioning was systematically verified at autopsy.

### **Measurement Apparatus**

In order to obtain data from prolonged recordings (with periods of wakefulness and sleep) in lambs, we used our recently developed and specifically designed radiotelemetry system (10). The transmitter used in this study was composed of 8 differential channels for nasal flow, ECG, EOG, EEG and 4 EMG recordings. The eight transmitted signals were fed from the receiver to the acquisition system. The raw EMG signals were rectified, integrated and averaged (moving time average of 100 ms). Constant acquisition of the SaO<sub>2</sub> was possible with the use of a pulse oximeter transmitting its signals also by a specific radiotelemetry system (17). Qualitative assessment of thoracic and abdominal movements and of lung volume variations was monitored in all lambs with the use of respiratory inductance plethysmography (Respirace, NIMS, Miami Beach, FL). A custom-made nasal mask was built to fit the muzzle of each lamb as followed. First on, we made a mould of the lamb muzzle with the use of an aluminium padded, malleable splint (Sam-splint, CDMV, St-Hyacinthe, QC, Canada). This mould was modified to allow the fastening of a double nasal cannula (4.5 endotracheal tube

cut and filled) and of a nasogastric tube (8 French). The mould was then covered by strips of plaster to obtain a solid shell. Once dried, the splint was removed from the shell, which was attached behind the lamb's head with a cotton ribbon. The mask was then filled with dental paste (Examix # 138006, Servident, St-Laurent, QC, Canada) to assure nasal ventilation without air leakage. Of note, the nasal mask did not impede mouth opening, in an attempt to not interfere with NNS. Nasal ventilation was performed using a Siemens Servo 300 mechanical ventilator with heated (33°C), humidified air. Finally, the CPAP/IPPV values were monitored continuously, using a calibrated pressure transducer (MP 45-30-871, Validyne, Northridge, CA) connected to the inspiratory circuit of the ventilator. An observer was always present with the lamb to note all events occurring during the recordings. Polysomnographic signals were recorded on a PC computer (Pentium 3) using a computerized acquisition device (MP150, Biopac Systems, Santa Barbara, CA) and software (Acknowledge 3.7.3, Biopac Systems Inc.). Collected data were stored on compact disk for further analysis.

### **Design of the study**

Upon arrival in our animal quarters, the lambs were cared without their mother. They were fed *ad libitum* three times a day with ewe's milk at 8:00 am, 1:00 and 6:00 pm and thrived normally. Surgical instrumentation was performed on the second day of life. Polysomnographic recordings of 4 to 6 hours were performed on three consecutive days at 4, 5 and 6 days of life, between 2:00 and 8:00 pm. Lights were off throughout the recordings. Each lamb was studied without

sedation. On experimental days, the lamb was fed freely at 8:00 am, received only 100 ml at 1:00 pm (to prevent accumulation of milk in the stomach, which could prevent evacuation of air by the nasogastric tube) and was fed freely at the end of the polysomnographic recordings. Three different ventilatory modes were tested in random order using the nasal mask + nasogastric tube, including no CPAP cm H<sub>2</sub>O (control), CPAP 6 cm H<sub>2</sub>O (nCPAP 6) and IPPV 10/4 cm H<sub>2</sub>O (nIPPV 10/4).

### **Data analysis**

All signals were carefully observed and analyzed throughout the recordings in relation with the states of alertness. Standard electrophysiological and behavioral criteria were used to define wakefulness (W), quiet sleep (QS), active sleep (AS) and arousal, as previously described (19). NNS activity was recognized by a brief, high amplitude TA EMG burst, as previously validated (16). NNS activity was then characterized either as an isolated NNS, or a burst of NNS, which was defined for the purpose of this study as 2 or more NNS occurring within a period of 4 sec (more than 90% of NNS bursts were comprised within a 4 sec time period). In a first analysis, NNS frequency (number of NNS per hour) was calculated for isolated NNS, bursts of NNS and total NNS (isolated + bursts of NNS), for each state of alertness and in each ventilatory mode. NNS occurring during active wakefulness was not analyzed because of motion artefacts, which prevented us to analyze TA EMG signal. Thus, calculation of NNS frequency during wakefulness was restricted to periods of quiet wakefulness. Secondly,

diaphragmatic EMG and the sum signal of the respiratory inductance plethysmography were used to recognize the phase of the respiratory cycle disrupted by isolated NNS. Each isolated NNS activity was then defined depending on the respiratory phase preceding and following NNS. Four types of isolated NNS were described (16): *e*-type NNS (preceded and followed by an expiration), *ei*-type NNS (at the transition from expiration to inspiration), *i*-type NNS (preceded and followed by an inspiration) and *ie*-type NNS (at the transition from inspiration to expiration). Only NNS with good quality diaphragmatic EMG and respiratory inductance plethysmography signals were analyzed for this purpose. NNS frequency was then calculated for each type of isolated NNS, in each state of alertness and in each ventilatory mode.

### **Statistical analysis**

Statistical analyses were performed using the SAS software. For quantitative variables, summary results are expressed as mean and standard deviation (SD). Results on NNS frequency were first averaged for each lamb and then averaged for the entire group of 12 lambs as a whole. The effects of nasal ventilation, state of alertness as well as coordination between NNS and the respiratory cycle were tested by generalized linear models with repeated measures (GENMOD procedure). Generalized linear models consisted in Poisson regression models for count data, while repeated measures ANOVA was used for blood gas analyses. A value of  $P < 0.05$  was considered as statistically significant.

## **RESULTS**

### **General results**

**Animals.** Twelve lambs weighing 4.2 kg (SD 0.9) (range 3.1 to 6.1) on the day of surgery were included in the study. One lamb was ultimately excluded because it did not sleep during the recordings. Analyses were therefore carried out in 11 lambs in control conditions, 10/11 with nCPAP 6 and 10/11 with nIPPV 10/4 (technical problems being responsible for the absence of one lamb in the last two groups).

**Blood gas analyses.** No statistical differences were observed between arterial blood gas parameters taken prior to installation of the nasal mask and at the end of the experiment, regardless of nasal pressure applied. Values before and after recordings were respectively: pH = 7.47 (SD 0.03) and 7.46 (SD 0.02), PaO<sub>2</sub> = 72 (SD 10) and 76 (SD 9) Torr, PaCO<sub>2</sub> = 35 (SD 3) and 35 (SD 5) Torr; HCO<sub>3</sub><sup>-</sup> = 26 (SD 3) and 25 (SD 4) mmoles/L.

**States of alertness.** Total duration of polysomnographic recordings was 141.4 h, with a mean recording time of 4.2 h (SD 0.7) (range 2.2 to 6.3) for each experimental condition in each lamb. Mean duration of states of alertness in each lamb was 2.4 h (SD 0.7) (range 1.6 to 3.5) in W, 1.3 h (SD 0.4) (range 0.4 to 2.4) in QS and 0.1 h (SD 0.1) (range 0 to 0.5) in AS. Distribution of states of alertness was identical among all 3 ventilatory modes. The three states of alertness were present in all but two lambs, for which no AS was observed during the control recording. Sample tracings obtained in a lamb with nCPAP 6 are given in figure 1.

### **NNS frequency in control conditions**

The effects of the states of alertness on NNS frequency in control conditions are illustrated in figure 2B. First, total NNS frequency was significantly higher in AS [174 h<sup>-1</sup> (SD 72) (range 50-302)] and quiet W [63 h<sup>-1</sup> (SD 22) (range 33-108)] than in QS [36 h<sup>-1</sup> (SD 14) (range 12-58)]. In addition, total NNS frequency was significantly higher in AS than in quiet W. Similarly, isolated NNS frequency was significantly higher in AS [88 h<sup>-1</sup> (SD 25) (range 50 to 114)] and quiet W [58 h<sup>-1</sup> (SD 15) (range 33 to 87)] than in QS [35 h<sup>-1</sup> (SD 15) (range 12 to 58)]. Isolated NNS frequency was also significantly higher in AS than quiet W. Finally, the same picture was seen for NNS bursts, which occurred significantly more often during AS (32 h<sup>-1</sup> (SD 20)) and quiet W (2 h<sup>-1</sup> (SD 3)) than during QS (0.3 h<sup>-1</sup> (SD 0.5)). In addition, NNS bursts were significantly more frequent in AS than in quiet W. All P values for the above analyses were equal or inferior to 0.0004.

### **Effects of nasal application of positive airway pressure on NNS frequency**

In all cases, lambs with nCPAP 6 or nIPPV 10/4 exhibited similar patterns in NNS frequency with regard to their distribution among the three states of alertness, comparatively to that observed in lambs in control conditions (Fig. 2B).

**Total NNS.** Results are illustrated in figure 2A and 2B, top panel. Compared to control conditions, nCPAP 6 inhibited NNS in 5/10 lambs during quiet W, 9/10 lambs during QS and 3/8 lambs during AS (P = 0.03, QS vs. quiet W). In addition, when all three states of alertness were grouped together, nCPAP 6

decreased overall NNS frequency ( $P = 0.02$ ). This decrease in NNS was statistically significant during QS ( $P < 0.0001$ ), but not during quiet W ( $P = 0.07$ ) or AS ( $P = 0.2$ ). Meanwhile, nIPPV 10/4 inhibited NNS in 6/10 lambs during quiet W, 8/10 lambs during QS and 4/8 lambs during AS, as compared to control conditions. However, the magnitude of this inhibition was lower than that observed with nCPAP 6, and was not statistically significant when all states of alertness were grouped together ( $P = 0.8$ ). On the other hand, this decrease in total NNS by nIPPV 10/4 did reach borderline significance during quiet W ( $P = 0.05$ ), but not during AS ( $P = 0.7$ ) and QS ( $P = 0.5$ ). Overall, nCPAP 6 had significantly greater inhibiting effects on total NNS than nIPPV 10/4 during QS ( $P = 0.0002$ ). No statistical difference was noted between nCPAP 6 and nIPPV 10/4 for both quiet W ( $P = 0.9$ ) and AS ( $P = 0.3$ ).

**Isolated NNS.** Results are illustrated in figure 2A and 2B, middle panel. As compared to control conditions ( $51 \text{ h}^{-1}$  (SD 14)), nCPAP 6 ( $37 \text{ h}^{-1}$  (SD 10)) decreased isolated NNS frequency ( $P = 0.0008$ ), when all states of alertness were grouped together. As in total NNS, this decrease in isolated NNS frequency was statistically significant during QS ( $P < 0.0001$ ), but not during quiet W ( $P = 0.1$ ) or AS ( $P = 0.6$ ). Conversely, nIPPV 10/4 ( $43 \text{ h}^{-1}$  (SD 14)) did not significantly decrease isolated NNS frequency, as compared to control conditions, when combining all states of alertness ( $P = 0.06$ ). Further analyses revealed that nIPPV 10/4 decreased isolated NNS frequency during quiet W ( $P = 0.05$ , *i.e.*, borderline significance) but increased their frequency during AS ( $P = 0.04$ ). No significant effect was observed during QS ( $P = 0.5$ ). Overall, the



inhibiting effects of nCPAP 6 on isolated NNS were significantly greater than that of nIPPV 10/4 during QS ( $P = 0.0003$ ). No statistical difference was noted between nCPAP 6 and nIPPV 10/4 for both quiet W ( $P = 1$ ) and AS ( $P = 0.2$ ).

**Bursts of NNS.** Results are illustrated in figure 2A and 2B, bottom panel. Compared to control conditions ( $3 \text{ h}^{-1}$  (SD 3)), nCPAP 6 ( $2 \text{ h}^{-1}$  (SD 2)) did not decrease NNS burst frequency, when all states of alertness were grouped together ( $P = 0.8$ ). However, further analysis revealed that nCPAP 6 significantly decreased NNS burst frequency during AS ( $P = 0.01$ ) but not during quiet W ( $P = 0.9$ ) or QS ( $P = 0.7$ ). By contrast, nIPPV 10/4 ( $1 \text{ h}^{-1}$  (SD 1)) decreased NNS burst frequency relative to control conditions ( $3 \text{ h}^{-1}$  (SD 3)), when all states of alertness were grouped together ( $P = 0.003$ ). A significant decrease in NNS burst frequency by nIPPV was observed during quiet W ( $P = 0.02$ ), but not during AS ( $P = 0.2$ ) or QS ( $P = 0.9$ ). Moreover, the inhibiting effects of nIPPV 10/4 on NNS burst frequency were statistically greater than those of nCPAP 6, when all states of alertness were grouped together ( $P < 0.0001$ ) and during quiet W ( $P = 0.0005$ ). Identical results were obtained when comparing the effects of nCPAP 6 and nIPPV 10/4 on the average number of NNS within a burst.

**In summary**, both the states of alertness and the application of positive airway pressure influenced NNS frequency. The main effects can be summarized as follows. First, the highest NNS frequency was consistently observed in AS, and the lowest one in QS, whatever the experimental condition and the type of NNS (total, isolated or in bursts). Secondly, the overall effect of nCPAP 6 was inhibitory on NNS, and was observed in QS for isolated NNS and in AS for bursts

of NNS. Thirdly, the effect of nIPPV 10/4 on NNS frequency was more variable, being an overall decrease in NNS in quiet W, but an increase in isolated NNS in AS.

### **Coordination between NNS and phases of the respiratory cycle**

Results on the coordination between NNS and phases of the respiratory cycle are illustrated in figure 3.

**Control conditions.** During quiet W in control conditions, *i*-type NNS [ $26 \text{ h}^{-1}$  (SD 14), 43%] and *ei*-type NNS [ $20 \text{ h}^{-1}$  (SD 10), 32%] were the most frequent. Both these NNS types were significantly more frequent than the *ie*-type [ $11 \text{ h}^{-1}$  (SD 5), 19%]. Finally, *e*-type NNS [ $4 \text{ h}^{-1}$  (SD 3), 8%] were the least common, significantly less than the 3 other NNS types. This pattern of NNS-respiration coordination was similar for both QS and AS as well. All of the above P values were inferior to 0.002.

**nCPAP 6.** Overall, during the three states of alertness, the same pattern of NNS-respiration coordination was observed with nCPAP 6 than in control conditions. The only difference was an absence of statistical difference with nCPAP 6 between *ie*-type and *e*-type NNS during AS. In addition, a statistically significant decrease in *ei*-type NNS was noted with nCPAP 6 during quiet W ( $P = 0.006$ ). Similarly, a statistically significant decrease in *i*-type NNS ( $P = 0.04$ ), *ei*-type and *ie*-type NNS ( $P < 0.0001$ ) and *e*-type NNS ( $P = 0.03$ ) was noted with nCPAP 6 during QS. Finally, only the *ie*-type NNS ( $P = 0.02$ ) exhibited a statistically significant decrease with nCPAP 6 during AS.

**nIPPV 10/4.** Overall, during the three states of alertness, the pattern of NNS-respiration coordination was largely similar to that observed for both control conditions and nCPAP 6, with again an absence of statistical difference with nIPPV 10/4 between *ie*-type NNS and *e*-type NNS during AS. Further analyses showed a statistically significant decrease in *i*-type NNS ( $P = 0.02$ ) between control conditions and nIPPV 10/4 during quiet W. Conversely, in comparison with no-CPAP, the *ei*-type NNS were significantly increased during nIPPV 10/4 during AS ( $P = 0.03$ ); the latter condition was the only exception in the pattern of NNS-respiration coordination, with the *ei*-type tending to be more frequent than the *i*-type.

**In summary,** overall, nCPAP 6 and nIPPV 10/4 had virtually no effect on the coordination between NNS and phases of the respiratory cycle. The increase in the *ei*-type with nIPPV 10/4 appeared as an exception.

## **DISCUSSION**

### **Statement of principal findings**

The present study brings new knowledge on the effect of application of positive airway pressure *via* a nasal mask on spontaneous, non-nutritive swallowing activity in the neonatal period. First, the results provided herein confirm that nasal CPAP significantly decreases NNS frequency, and show that the sleep states have a modulating effect, with inhibition of isolated NNS during QS and of bursts of NNS in AS. Secondly, unique results on nasal IPPV show that its effects on NNS frequency are more variable, with an inhibition of NNS only in quiet W, and an increase in isolated NNS frequency in AS. Thirdly, the present results also demonstrate that nasal positive airway pressure does not alter the coordination between NNS and phases of the respiratory cycle. Finally, use of a nasal mask and naso-gastric tube does not modify NNS frequency or its coordination with phases of the respiratory cycle. Relevance of the present results mainly stems from the importance of NNS for clearing airway secretions and gastric content regurgitated from the stomach, which contributes to the prevention of apnea, bradycardia and hypoxemia events in the newborn.

### **Inhibition of NNS frequency by nasal application of positive pressure**

While a previous study reported an inhibition of water-induced swallows by nasal CPAP in conscious adult humans (13), studies documenting the effects of nasal CPAP or IPPV on spontaneous NNS are currently non-existent. Thus, the present observation in the newborn lamb that nCPAP 6 inhibits NNS frequency

more than nIPPV 10/4 during sleep is a significant finding. However, the mechanisms responsible for NNS inhibition during nasal application of positive airway pressure remain unclear. A decrease in upper airway secretions by a drying effect of positive pressure application is unlikely, due to the use of humidified air. In addition, this drying effect would likely be more prominent with nIPPV 10/4 than with nCPAP 6, due to greater convection effects with nIPPV, hence leading to a stronger NNS inhibition than with nCPAP, which is contrary to the present results, at least in sleep. Other hypotheses also come to mind. First, inhibition of the swallowing reflex could be elicited by the stimulation of pressure receptors located in the upper airways, especially in the laryngeal mucosa. These receptors, whose activity is modulated by the application of negative or positive pressure in the upper airways, account for the majority (~60%) of receptors described in the laryngeal region (12, 20). Stimulation of positive pressure receptors of the laryngeal region by application of nasal ventilatory support could therefore trigger inhibitory afferent messages relayed to the swallowing centers in the brainstem. Recent studies have shown that direct application of continuous or intermittent positive pressure on the isolated piglet larynx modulates the activity of laryngeal muscles. Interestingly, the effects on laryngeal muscle activity were more important with continuous than with intermittent application of positive pressure, similarly to our present observations (21). Further studies assessing the effects of positive pressure applied *via* a tracheostomy in spontaneously breathing lambs, and therefore without stimulation of upper airway receptors, should enable to verify this hypothesis.

Secondly, NNS inhibition could be elicited by stimulation of slow adapting bronchopulmonary receptors, since the administration of nasal ventilatory support is associated with lung inflation. Stimulation of these receptors by nasal ventilation would thereby inhibit swallowing by a vagally-mediated lung reflex. In support of this hypothesis, continuous lung inflation brought about by application of continuous negative extrathoracic pressure in awake adult humans significantly inhibits water-triggered swallowing activity (9). In addition, voluntary hyperpnea (hypocapnic or normocapnic) was shown to inhibit water-induced swallowing in awake adult humans (24). This hypothesis will need further testing by repeating the present study in vagotomized lambs. Finally, given that NNS appear to be triggered when piriform sinuses are full, distension of the latter by application of positive pressure in the upper airways could delay filling and decrease NNS frequency (BT Thach, personal communication). Further studies by applying CPAP through a tracheostomy should allow to test this hypothesis. Regardless of the mechanism(s) involved, it is clear that nCPAP 6, and to a lesser degree nIPPV 10/4, inhibit NNS in the newborn lamb.

### **Coordination between NNS and phases of the respiratory cycle**

A perfect coordination between swallowing and respiratory activity is necessary to minimize the risk of aspiration or prolonged apneas, especially in vulnerable infants, such as preterm newborns. The present study illustrates that, overall, nasal application of positive pressure ventilation in newborn lambs does not modify the coordination between NNS and phases of the respiratory cycle, *i.e.*,

that the *i-type* NNS is the most frequent, and the *e-type* NNS the least frequent. This observation may seem somewhat surprising in newborn lambs, given previous observations of altered coordination between swallowing and phases of the respiratory cycle in adult humans in various experimental conditions, including imposed hypercapnia (14), respiratory elastic loading (8), lung inflation due to negative extrathoracic pressure (9) and voluntary hyperpnea (24). While we cannot provide any clear explanations for what might be considered as discrepant results, important differences between experimental conditions in lambs versus adults should be emphasized however, including experimental maneuvers used to impose respiratory changes, the presence of full consciousness throughout the experiments in humans (and thus awareness of the maneuvers), and the study of water-triggered swallowing in humans vs. spontaneous NNS in lambs. Finally, species differences, including body position (erect/sitting vs. on all fours/supine) cannot be ruled out.

### **Absence of effects of nasal mask and/or naso-gastric tube on non-nutritive swallowing**

Given preliminary personal observations that nasal application of positive pressure ventilation in newborn lambs led to important gastric distension, the use of a naso-gastric tube in the present experiments was deemed mandatory, although there were concerns that the use of a nasal mask and/or a naso-gastric tube might alter NNS. Comparison of present observations with nasal mask + naso-gastric tube, but without CPAP (*i.e.*, what we call control conditions herein),

with previous results obtained in our laboratory in lambs of the same age, but without mask or naso-gastric tube, reveal similar results, notably with regard to NNS frequency, NNS-respiratory coordination and the effects of sleep states (16).

### **Clinical relevance of present findings**

In addition to the physiological knowledge gained from the present study, the data also has clear and relevant clinical implications, especially with regard to preterm newborn infants, who at times must spend numerous weeks on nasal CPAP for treatment of recurrent apneas. Indeed, the observed decrease in NNS frequency may have deleterious effects in newborn infants under nasal CPAP treatment, by an increased risk of aspirating saliva or regurgitated gastric content. In addition, the inhibitory effect on NNS may impact on swallowing maturation, due to high brain plasticity in very immature infants. While highly speculative, consequences of this might range from delays in swallowing maturation or, more seriously, translate into prolonged abnormalities of swallowing activity. However, the virtual absence of alterations in the coordination between NNS and phases of the respiratory cycle is somewhat reassuring. In addition, the absence of deleterious effects of nasal mask and naso-gastric tube, especially considering that the latter is used in all preterm infants born prior to 35 weeks of gestational age, is of significant clinical relevance.



In conclusion, the present study illustrates for the first time that NNS is inhibited by nasal application of positive airway pressure in newborn lambs, especially by CPAP 6 during sleep and IPPV 10/4 during quiet W. While this finding could have important clinical implications for maturation of swallowing activity, elucidation of the mechanisms responsible for this inhibition awaits further study.

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## **FIGURE LEGENDS**

**Figure 1** : A) Spontaneous and isolated non-nutritive swallowing (*i*-type NNS) occurring during quiet sleep B) burst of NNS occurring during active sleep in the same full term lamb during administration of nasal CPAP 6 cm H<sub>2</sub>O. Abbreviations from top to bottom: TA, raw thyroarytenoid EMG signal; ∫TA, integrated TA; Di, raw diaphragmatic EMG signal; ∫Di, integrated Di; Sum, sum signal of the respiratory inductance plethysmography (inspiration upwards); EEG, electroencephalogram; EOG, electrooculogram.

**Figure 2** : Relationship between NNS frequency (number of NNS per hour) and the different ventilatory conditions studied [no CPAP (Cont.), CPAP 6 (6), IPPV 10/4 (10/4) cm H<sub>2</sub>O] when A) all states of alertness are taken together and B) each state of alertness is considered individually. Top panel illustrates results for total NNS frequency, middle panel illustrates results for isolated NNS frequency and bottom panel illustrates results for NNS burst frequency. Please note the different scale for the y axis. W: wakefulness; QS: quiet sleep; AS: active sleep. Results are presented as mean (SD). \* : P < 0.05; ‡: P < 0.05, nCPAP 6 vs. no CPAP; £: P < 0.05, nIPPV 10/4 vs. no CPAP and \*\* : P < 0.05, nIPPV 10/4 vs. nCPAP 6.

**Figure 3** : Absence of systematic differences between control conditions (top panel), nCPAP 6 (middle panel) and nIPPV 10/4 (bottom panel) cm H<sub>2</sub>O regarding the coordination between NNS and respiratory phases in quiet W, QS and AS. Abbreviations: *i*-type NNS, NNS beginning and ending in inspiration; *ie*-type NNS, NNS beginning in inspiration and ending in expiration; *ei*-type NNS, NNS beginning in expiration and ending in inspiration; *e*-type NNS, NNS beginning and ending in expiration. Results are presented as mean (SD). \* : P < 0.05, *i*-type NNS vs. *ie*-type NNS; Δ : P < 0.05, *i*-type NNS vs. *ei*-type NNS; ∙ : P < 0.05, *i*-type NNS vs. *e*-type NNS; □ : P < 0.05, *ie*-type NNS vs. *ei*-type NNS; ♥ : P < 0.05, *ie*-type NNS vs. *e*-type NNS; ∙ : P < 0.05, *ei*-type NNS vs. *e*-type NNS; ‡ : P < 0.05, nCPAP 6 vs. no CPAP; £ : P < 0.05, nIPPV 10/4 vs. no CPAP; \*\* : P < 0.05, nIPPV 10/4 vs. no CPAP. Please note that, for reasons of clarity, no symbols have been added to illustrate the significant effects of the states of alertness. These effects are described in the results section of the article.

# FIGURES

Figure 1

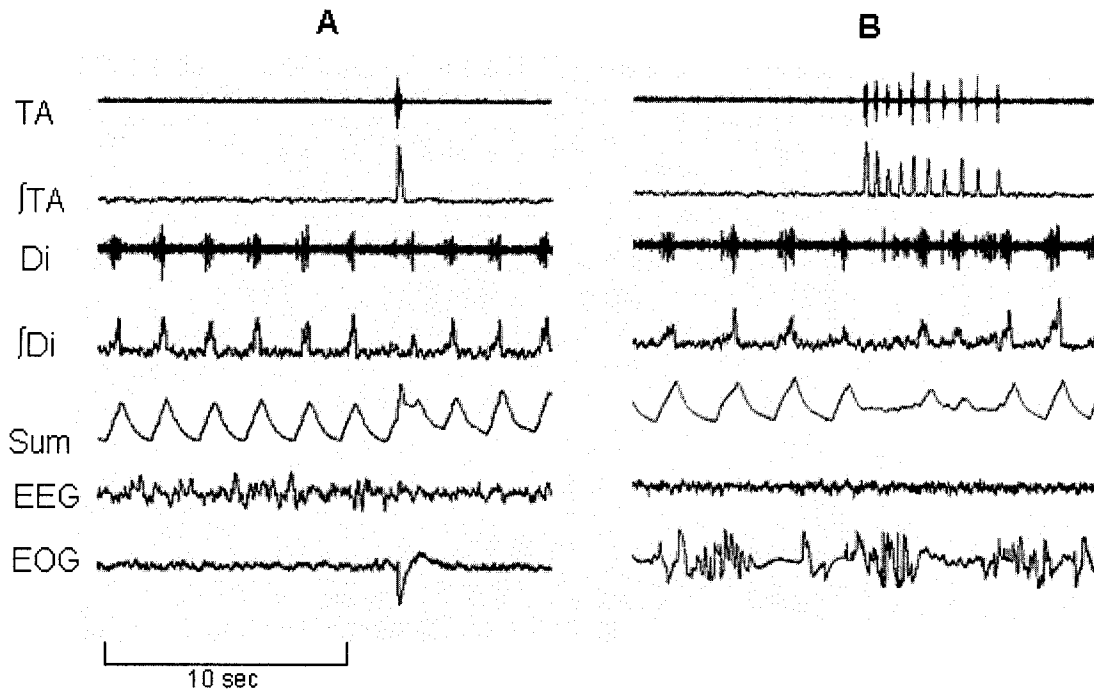




Figure 2

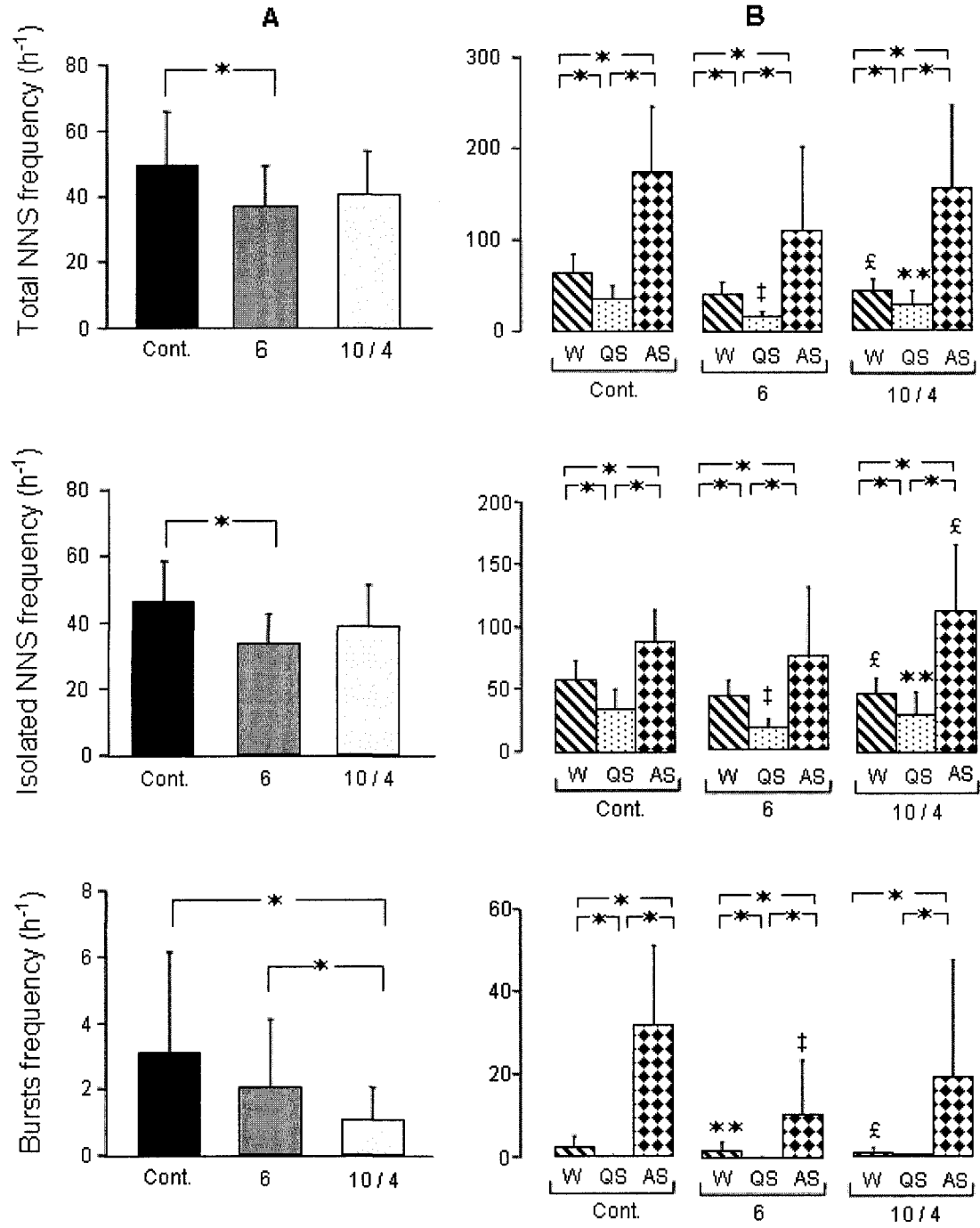
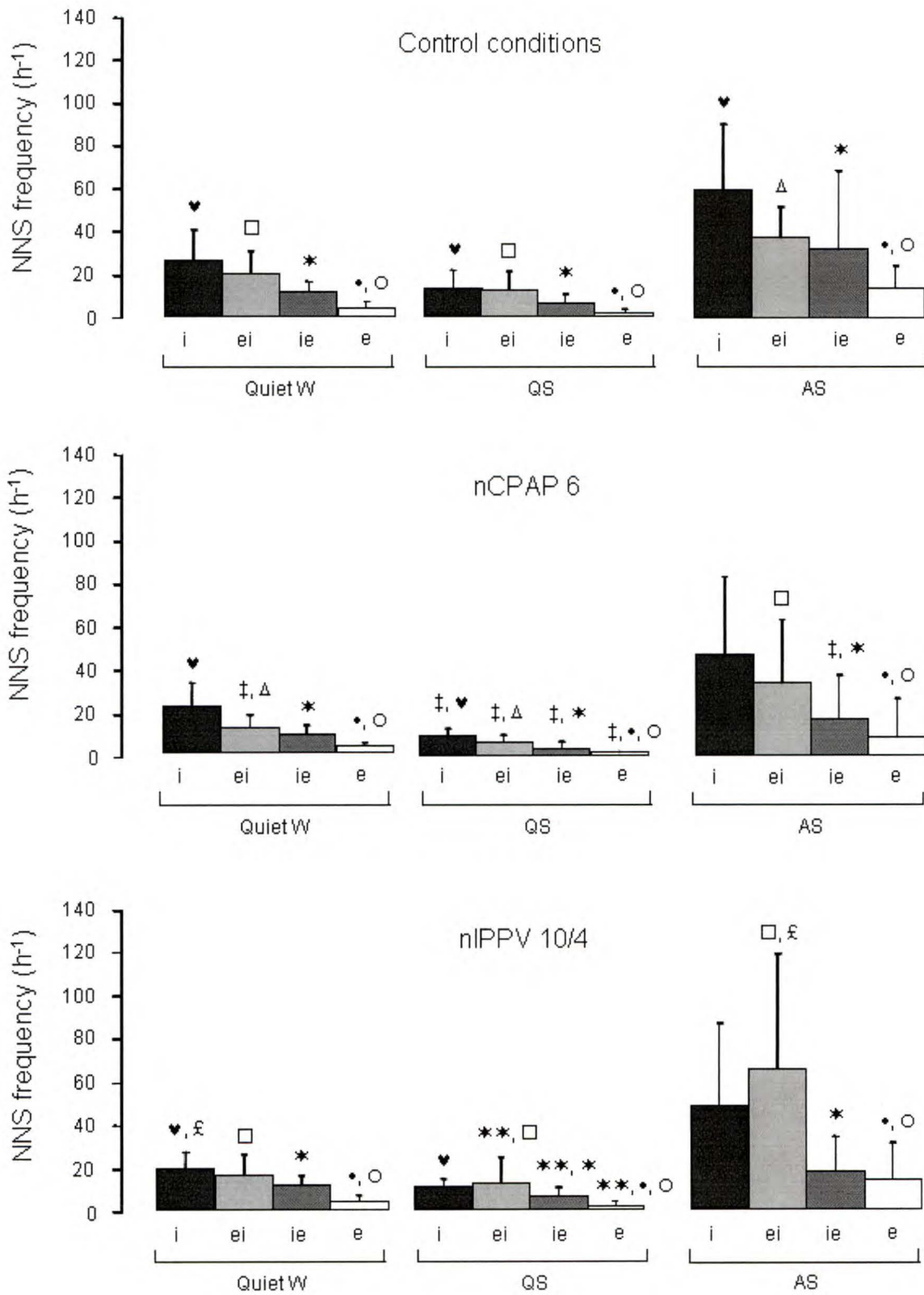


Figure 3



## **DISCUSSION**

La présente étude élargit nos connaissances très limitées sur l'effet de l'application d'une pression positive *via* un masque nasal sur le réflexe de déglutition. Elle nous fournit également de nouvelles connaissances sur l'effet de l'application d'une pression positive sur la coordination entre DNN et les phases de la respiration durant les divers stades de conscience. Ainsi, les résultats uniques de cette étude montrent que globalement, la PPC diminue significativement la fréquence des DNN (nombre de DNN / heure), plus spécifiquement les DNN isolées en sommeil calme et les DNN en bouffées en sommeil agité. En comparaison, les effets de la VPPI sont plus variables, avec une diminution significative de la fréquence des DNN à l'éveil seulement, et une augmentation significative de la fréquence des DNN isolées en sommeil agité. De plus, ces résultats démontrent que l'application nasale d'une pression positive ne perturbe pas la coordination fine entre les DNN et les phases du cycle respiratoire. Finalement, cette étude suggère que l'utilisation d'un masque nasal et d'un tube naso-gastrique ne modifie pas la fréquence des DNN, sa coordination avec les phases du cycle respiratoire et l'effet des stades de conscience.

## **Pertinence clinique de nos découvertes**

En plus des nouvelles connaissances physiologiques acquises par cette étude, nous pensons que ces nouvelles découvertes ont une pertinence clinique, particulièrement pour les enfants nés prématurément qui, quelquefois, doivent passer de nombreuses semaines avec une PPC nasale afin de traiter leurs apnées récurrentes. Ainsi, l'observation d'une diminution de la fréquence des DNN peut avoir des effets délétères chez les nourrissons sous traitement par PPC nasale, en augmentant le risque d'aspiration salivaire ou de reflux du contenu gastrique. De plus, bien que ceci soit hypothétique, l'inhibition prolongée de la fonction de déglutition pourrait avoir un impact sur la maturation de cette fonction, dû à la plasticité importante du cerveau en période néonatale. Ainsi, la modification de la fonction de déglutition suite à l'application d'une pression positive peut tout simplement retarder la maturation de cette fonction ou induire un développement anormal du réflexe de déglutition (nutritive et/ou non-nutritive) qui peut laisser des séquelles. Par contre, l'absence de modifications de la coordination entre les DNN et les phases du cycle respiratoire est quelque peu rassurante. De plus, l'absence d'effets du masque nasal et du tube nasogastrique, le dernier étant utilisé chez tous les enfants prématurés nés avant 35 semaines d'âge gestationnel, est d'une importance clinique capitale.

## **Limitations et perspectives de l'étude**

Cette étude comprend certaines limitations. Tout d'abord, nous n'étudions que quelques heures d'application de la pression positive (exposition aiguë),

alors que les nouveaux-nés vont souvent avoir l'application nasale de cette pression positive en permanence durant plusieurs semaines. Ainsi, nos résultats ne nous permettent donc pas de déterminer quelles sont les séquelles éventuelles de l'application à long terme (exposition chronique) d'une pression positive nasale. Deuxièmement, chez les nouveaux-nés sous support ventilatoire nasal, d'autres anomalies peuvent s'ajouter, telles de l'hypoxie et de l'hypercapnie, anomalies qui peuvent aussi influencer les DNN. Troisièmement, cette étude a été réalisée seulement chez des agneaux nés à terme. Ainsi, certaines différences pourraient être identifiées suite à l'exécution de ce protocole sur notre modèle d'agneaux nés prématurément. Par contre, toutes ces limitations ne doivent pas faire oublier que notre étude est la première à identifier les effets de l'application nasale d'une pression positive sur les DNN.

### **Perspectives**

Plusieurs études sont prévues à court et moyen terme comme suite à ce travail. Tout d'abord, les études à court terme devront tenter de déterminer les mécanismes expliquant l'inhibition des DNN suite à l'application d'une PPC. Pour tester les hypothèses évoquées dans la discussion de l'article, nous étudierons donc des agneaux trachéotomisés et des agneaux vagotomisés. L'influence de l'hypoxie et de l'hypercapnie sur la fréquence basale des DNN et la coordination fine des DNN avec les phases du cycle respiratoire sera aussi étudiée prochainement dans notre laboratoire. Enfin, à moyen terme, nous prévoyons d'étudier d'autres conditions qui peuvent perturber les DNN chez les nouveaux-

nés, en particulier différents types d'inflammation des voies aériennes supérieures telles que les laryngites de reflux gastro-oesophagien, l'infection par le virus respiratoire syncytial ou l'exposition à la fumée de cigarette.

## **CONCLUSION**

En conclusion, notre étude montre pour la première fois que les DNN sont inhibées par l'application nasale d'une ventilation à pression positive chez les agneaux nouveau-nés et, ceci particulièrement par la PPC durant le sommeil. Malgré le fait que nous ne connaissons pas la réelle implication clinique de l'utilisation chronique de cette ventilation auprès des enfants prématurés, ces nouvelles découvertes ont une pertinence clinique importante pour la maturation de l'activité de déglutition. Par contre, le mécanisme responsable de cette inhibition nécessite de plus amples investigations.

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