



**HAL**  
open science

## **Pediatric long-term noninvasive respiratory support in children with central nervous system disorders**

Marion Carrara, Guillaume Aubertin, Sonia Khirani, Bruno Massenavette, Priscille Bierme, Lucie Griffon, Iulia Ioan, Cyril Schweitzer, Alexandra Binoche, Marie-emilie Lampin, et al.

### ► To cite this version:

Marion Carrara, Guillaume Aubertin, Sonia Khirani, Bruno Massenavette, Priscille Bierme, et al.. Pediatric long-term noninvasive respiratory support in children with central nervous system disorders. *Pediatric Pulmonology*, 2023, 10.1002/ppul.26796 . hal-04343909

**HAL Id: hal-04343909**

**<https://hal.science/hal-04343909>**

Submitted on 2 Feb 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# **Pediatric long-term noninvasive respiratory support in children with central nervous system disorders**

Marion Carrara <sup>1</sup>, Guillaume Aubertin <sup>1 2 3</sup>, Sonia Khirani <sup>4 5 6</sup>, Bruno Massenavette <sup>7</sup>, Priscille Bierme <sup>8</sup>, Lucie Griffon <sup>4 5</sup>, Iulia Ioan <sup>9</sup>, Cyril Schweitzer <sup>9</sup>, Alexandra Binoche <sup>10</sup>, Marie-Emilie Lampin <sup>10</sup>, Clémence Mordacq <sup>11</sup>, Robert Rubinsztajn <sup>12</sup>, Stéphane Debeilleix <sup>13</sup>, François Galode <sup>13</sup>, Stéphanie Bui <sup>13</sup>, Eglantine Hullo <sup>14</sup>, Arnaud Becourt <sup>15</sup>, Marc Lubrano <sup>16</sup>, Johan Moreau <sup>17 18</sup>, Marie-Catherine Renoux <sup>17</sup>, Stefan Matecki <sup>17 19</sup>, Nathalie Stremmer <sup>20</sup>, Melisande Baravalle-Einaudi <sup>20</sup>, Julie Mazenq <sup>20</sup>, Elodie Sigur <sup>21</sup>, Géraldine Labouret <sup>21</sup>, Anne-Laure Genevois <sup>21</sup>, Rachel Heyman <sup>22</sup>, Michael Pomedio <sup>23</sup>, Alexandra Masson <sup>24</sup>, Pauline Hangard <sup>24</sup>, Céline Menetrey <sup>24</sup>, Laurence Le Clainche <sup>25</sup>, Plamen Bokov <sup>25 26</sup>, Benjamin Dudoignon <sup>25</sup>, Emmanuelle Florence <sup>27</sup>, Jean Bergounioux <sup>28</sup>, Blaise Mbieleu <sup>28</sup>, Audrey Breining <sup>29</sup>, Lisa Giovannin-Chami <sup>30</sup>, Agnes Fina <sup>30</sup>, Morgane Ollivier <sup>31</sup>, Elsa Gachelin <sup>32</sup>, Caroline Perisson <sup>33</sup>, Anne Pervillé <sup>34</sup>, Audrey Barzic <sup>35</sup>, Pierrick Cros <sup>35</sup>, Mickaël Jokic <sup>36</sup>, Guillaume Labbé <sup>37</sup>, Véronique Diaz <sup>38</sup>, Laurianne Coutier <sup>8</sup>, Brigitte Fauroux <sup>4 5</sup>, Jessica Taytard <sup>1 39</sup>

<sup>1</sup> Department of Pediatric Pulmonology, AP-HP, Hôpital Armand Trousseau, Paris, France.

<sup>2</sup> Sorbonne Université, INSERM UMR-S 938, Centre de Recherche Saint-Antoine (CRSA), Paris, France.

<sup>3</sup> Centre de pneumologie de l'enfant, Ramsay Générale de Santé, Paris, France.

<sup>4</sup> Pediatric Noninvasive Ventilation and Sleep Unit, AP-HP, Hôpital Necker-Enfants malades, Paris, France.

<sup>5</sup> Université Paris Cité, VIFASOM, Paris, France.

<sup>6</sup> ASV Santé, Gennevilliers, France.

<sup>7</sup> Pediatric Intensive Care Unit, Hospices Civils de Lyon, Hôpital Femme-Mère-Enfant, Bron, France.

<sup>8</sup> Pediatric Pulmonology and Allergology Unit, Hospices Civils de Lyon, Bron, France.

<sup>9</sup> Department of Pediatric, University Children's Hospital, CHRU Nancy; Université de Lorraine, DevAH, Nancy, France.

<sup>10</sup> Pediatric Intensive Care Unit, Hôpital Jeanne de Flandre, CHU Lille, Lille, France.

<sup>11</sup> Pediatric Pulmonology and Allergology Unit, Hôpital Jeanne de Flandre, CHU Lille, Lille, France.

<sup>12</sup> Department of Pediatric orthopedic surgery, Hôpital Necker-Enfants malades, Paris, France.

<sup>13</sup> Pediatric Pulmonology Unit, Hôpital Pellegrin-Enfants, Bordeaux, France.

- <sup>14</sup> Pediatric Pulmonology Unit, Hôpital Couple-Enfant, CHU Grenoble, Grenoble, France.
- <sup>15</sup> Pediatric Pulmonology Department, CHU Amiens Picardie, Amiens, France.
- <sup>16</sup> Respiratory Diseases, Allergy and CF Unit, Department of Pediatric, University Hospital Charles Nicolle, Rouen, France.
- <sup>17</sup> Department of Pediatric Cardiology and Pulmonology, Montpellier University Hospital, Montpellier, France.
- <sup>18</sup> Physiology and Experimental Biology of Heart and Muscles Laboratory-PHYMEDEXP, UMR CNRS 9214, INSERM U1046, University of Montpellier, Montpellier, France.
- <sup>19</sup> Functional Exploration Laboratory, University Hospital, Montpellier, France.
- <sup>20</sup> Pediatric Ventilation Unit, Department of Pediatric, AP-HM, Hôpital La Timone, Marseille, France.
- <sup>21</sup> Pediatric Pulmonology and Allergology Unit, Hôpital des Enfants, Toulouse, France.
- <sup>22</sup> Pediatric Unit, Department of Physical Medicine and Rehabilitation, Hôpital Pontchaillou, Rennes, France.
- <sup>23</sup> Pediatric Intensive Care Unit, American Memorial Hospital, CHU Reims, Reims, France.
- <sup>24</sup> Pediatric Unit, Hôpital de la Mère et de l'Enfant, Limoges, France.
- <sup>25</sup> Pediatric Noninvasive Ventilation Unit, AP-HP, Hôpital Robert Debré, Paris, France.
- <sup>26</sup> Université Paris Cité, INSERM NeuroDiderot, Paris, France.
- <sup>27</sup> ESEAN-APF, Health Center for Children and Adolescents, Nantes, France.
- <sup>28</sup> Pediatric Intensive Care Unit, AP-HP, Hôpital Raymond Poincaré, Garches, France.
- <sup>29</sup> Department of Pediatric, CHU Strasbourg, Strasbourg, France.
- <sup>30</sup> Department of Pediatric Pulmonology and Allergology, Hôpitaux pédiatriques de Nice CHU-Lenval, Nice, France.
- <sup>31</sup> Pediatric Intensive Care Unit, CHU Angers, Angers, France.
- <sup>32</sup> Department of Pediatric, CHU Félix Guyon, Saint Denis, La Réunion, France.
- <sup>33</sup> Department of Pediatric, CHU Sud Réunion, Saint Pierre, La Réunion, France.
- <sup>34</sup> Department of Pédiatries, Hôpital d'Enfants-ASFA, Saint Denis, La Réunion, France.
- <sup>35</sup> Department of Pediatric, CHU Brest, Brest, France.

<sup>36</sup> Pediatric Intensive Care Unit, CHU de Caen Normandie, Caen, France.

<sup>37</sup> Pediatric Pulmonology and Allergology Unit, CHU d'Estaing, Clermont-Ferrand, France.

<sup>38</sup> Department of Respiratory Physiology, CHU Poitiers, Poitiers, France.

<sup>39</sup> INSERM UMR-S 1158 "Neurophysiologie Respiratoire Expérimentale et Clinique", Sorbonne Université, Paris, France, Paris, France.

**Keywords:**

airway clearance; central nervous system disorder; children; continuous positive airway pressure; multiple disabilities; noninvasive ventilation.

# Abstract

## **Rationale:**

The use of long-term noninvasive respiratory support is increasing in children along with an extension of indications, in particular in children with central nervous system (CNS) disorders.

## **Objective:**

The aim of this study was to describe the characteristics of children with CNS disorders treated with long-term noninvasive respiratory support in France.

## **Methods:**

Data were collected from 27 French pediatric university centers through an anonymous questionnaire filled for every child treated with noninvasive ventilatory support  $\geq 3$  months on 1st June 2019.

## **Main results:**

The data of 182 patients (55% boys, median age: 10.2 [5.4; 14.8] years old [range: 0.3-25]) were collected: 35 (19%) patients had nontumoral spinal cord injury, 22 (12%) CNS tumors, 63 (35%) multiple disabilities, 26 (14%) central alveolar hypoventilation and 36 (20%) other CNS disorders. Seventy five percent of the patients were treated with noninvasive ventilation (NIV) and 25% with continuous positive airway pressure (CPAP). The main investigations performed before CPAP/NIV initiation were nocturnal gas exchange recordings, alone or coupled with poly(somno)graphy (in 29% and 34% of the patients, respectively). CPAP/NIV was started in an acute setting in 10% of the patients. Median adherence was 8 [6; 10] hours/night, with 12% of patients using treatment  $< 4$  h/day. Nasal mask was the most common interface (70%). Airway clearance techniques were used by 31% of patients.

## **Conclusion:**

CPAP/NIV may be a therapeutic option in children with CNS disorders. Future studies should assess treatment efficacy and patient reported outcome measures.

# 1 | INTRODUCTION

Central nervous system (CNS) disorders are a heterogeneous group of diseases with various malformative, metabolic, genetic or traumatic etiologies.<sup>1–8</sup> Sleep disordered breathing and chronic respiratory insufficiency are frequent in this population, as neural structures located in the brainstem, cerebellum or medulla involved in breathing are often impacted.<sup>6,9–14</sup> In case of severe obstructive sleep apnea (OSA) or nocturnal hypoventilation, continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV) may be indicated. Indeed, CPAP is an effective treatment for upper respiratory airway obstruction and NIV may assist or replace the defective respiratory muscles or central respiratory drive.<sup>15</sup>

Among CNS disorders, multiple disabilities encompass a large range of diseases of various severity and prognosis, with multiple factors that precipitate chronic respiratory insufficiency, such as repeated infections, ineffective cough, swallowing disorders or severe scoliosis.<sup>1</sup> In France, the incidence of multiple disabilities has been estimated between 0.50 and 0.70/1000 children.<sup>16,17</sup>

Despite recent national recommendations, there is still a lack of consensus on respiratory management in this population, especially regarding the use of ventilatory support and airway clearance techniques.<sup>1</sup>

The use of NIV has greatly developed in the past 10 years, and a recent national French cross-sectional study reported a 14-fold increase in the number of children treated with CPAP or NIV between 2000 and 2019.<sup>18</sup> This study showed an increase of the use of CPAP/NIV in children with CNS disorders.

The aim of the present study was to analyze the subgroup of children with CNS disorders of the 2019 national survey.<sup>18</sup>

## 2 | MATERIALS AND METHODS

### 2.1 | Patients

This is an ancillary study reporting data on children with CNS disorders. The initial study was a national cross-sectional survey performed among the French national pediatric NIV/CPAP network which gathers 27 pediatric university centers distributed among 24 cities.<sup>18</sup>

For the present survey, the detailed methodology has been published in the original article.<sup>18</sup> Data were collected through an anonymous questionnaire filled for every child presenting with a CNS disorder, under noninvasive ventilatory support (NIV or CPAP) for more than 3 months on 1st June 2019. A small number of adult patients who were still followed in a pediatric center were also included in this study. The original study obtained the ethics committee approval (Comité d'Ethique de Necker Enfants malades, CENEM, No. CENEM19-5-BF) on March the 7th 2019, and all patients aged >6 years and parents gave their informed consent.

The following data were collected: age, gender, diagnosis, investigations performed before the NIV/CPAP initiation, parameters that led to the decision of NIV/CPAP treatment, NIV/CPAP duration, mean objective adherence to treatment during the last month obtained from the device built-in software, type of interface and NIV/CPAP device (life support ventilator: for use  $\geq 16$  h/24, full range of alarms, internal + external batteries  $\geq 8$  h and allows patient's mobility; intermediate: use between 8 and 16 h/24, basic alarms, internal battery  $\geq 2$  h; standard: use at night, no alarms, no battery), and the use of additional technologies such as supplemental oxygen therapy or airway clearance devices. The patients with CNS disorders were classified into five diagnostic groups: (1) multiple disabilities, (2) non-tumor spinal cord injury, (3) central alveolar hypoventilation, (4) CNS tumors and (5) others CNS diseases.

Disease group	Specific diagnosis	Number of patients
Nontumor spinal cord injury	Myelitis (±radiculitis or leukoencephalitis)	10
	Spinal dysraphism (spina bifida, Chiari malformation, myelomeningocele)	9
	Spinal cord injury	8
	Paraplegia or tetraparesis	6
	Syringomyelia	2
	<b>Total</b>	<b>35</b>
CNS tumors	Tumors of various locations (brainstem, spinal cord, encephalon) and histological types	16
	Neurofibromatosis	6
	<b>Total</b>	<b>22</b>
Multiple disabilities	Idiopathic neurodisability	38
	Genetic neurodisability:	22
	Rett syndrome	12
	West syndrome	2
	Other	8
	Neonatal encephalopathy	3
<b>Total</b>	<b>63</b>	
Central alveolar hypoventilation	CCHS	19
	Other central ventilator drive disorders	7
	<b>Total</b>	<b>26</b>
Other CNS disorders	Hypotonia	7
	Neuropathy	5
	Neurodevelopmental disorder	3
	Charcot-Marie-Tooth disease	3
	Hydrocephalus	3
	Williams-Beuren syndrome	2
	Cerebellar hypoplasia	2
	Brainstem disorder	2
	Friedreich ataxia	2
	Adrenoleukodystrophy	2
	Leukodystrophy	2
	Cerebral palsy	2
	Joubert syndrome	1
	<b>Total</b>	<b>36</b>

**TABLE 1** Specific diagnoses found in each group of children.

Abbreviations: CCHS, congenital central hypoventilation syndrome; CNS, central nervous system.

## 2.2 | Statistical analyses

Statistical analyses were performed using the pvalue.io Software. Descriptive statistics summarized patient's characteristics and NIV/CPAP technology. The variables were expressed as median [interquartile range, IQR]. Group comparisons were performed using the one way analysis of variance test or the Kruskal–Wallis one way analysis of variance on ranks test in case of nonparametric data. Comparisons between two groups were done using the ttest, or the Mann–Whitney Rank Sum test in case of nonparametric data. Comparisons of quantitative data were done using the Chi-square test. A p value <.05 was considered for significance.

# 3 | RESULTS

## 3.1 | Patients

One hundred and eighty-two patients with a median age of 10.2 [5.4; 14.8] years old at inclusion (range: 0.3–25 years old) treated with long-term NIV or CPAP were included in this study. The number of patients per center ranged from 0 to 20 patients. Nine patients (5%) were over 18 years old. Among these 182 children, 63 (35%) had multiple disabilities, 35 (19%) a non-tumor spinal cord injury, 22 (12%) a CNS tumor, 26 (14%) a central alveolar hypoventilation (CAH), and 36 (20%) other unclassified CNS diseases. The specific diagnoses found in each group of children are presented in Table 1.

TABLE 2 NIV/CPAP characteristics according to the diagnostic groups.

	Total population (n = 182, 100%)	Nontumor spinal cord injury (n = 35, 19%)	CNS tumors (n = 22, 12%)	Multiple disabilities (n = 63, 35%)	Central alveolar hypoventilation (n = 26, 14%)	Others CNS diseases (n = 36, 20%)
Age (years)	10.2 [5.4; 14.8]	8.7 [4.6; 4.4]	9.8 [6.4; 15.4]	13.3 [8.2; 15.4]	7.1 [5.4; 11.4]	9.8 [2.7; 14.8]
Age at initiation (years)	6.7 [2.3;12.0]	6.46 [3.39;11.4]	5.92 [3;10.5]	9.77 [5.4;12.9]	1.65 [0.1;5.6]	6.77 [1.3;12.8]
Sex ratio (M/F)	1.25	1.69	1.75	1.1	0.79	1.77
Male (n, %)	100 (55%)	22 (63%)	14 (64%)	32 (50%)	11 (42%)	23 (64%)
Female (n, %)	80 (44%)	13 (37%)	8 (36%)	30 (48%)	14 (54%)	13 (36%)
Missing data (n, %)	2 (1%)	0 (0%)	0 (0%)	1 (2%)	1 (4%)	0 (0%)
Duration of CPAP/ NIV (years)	1.9 [0.6; 3.8]	1.4 [0.3; 2.4]	3.8 [2.6;4.9]	1.7 [0.6; 3.5]	3.8 [1.01; 6.34]	1.3 [0.3;3.0]
Ventilatory mode						
NIV (n, %)	137 (75%)	31 (89%)	14 (64%)	44 (70%)	23 (88%)	25 (69%)
CPAP (n, %)	41 (23%)	4 (11%)	6 (27%)	18 (29%)	2 (8%)	11 (31%)
ASV (n, %)	3 (2%)	0 (0%)	2 (9%)	0 (0%)	1 (4%)	0 (0%)
Missing data (n, %)	1 (1%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)

Note: Data are expressed as median [Q1; Q3].

Abbreviations: ASV, adaptive servo-ventilation; CNS, central nervous system; CPAP, continuous positive airway pressure; NIV, noninvasive ventilation.

## 3.2 | Noninvasive ventilatory support

Median age at NIV/CPAP initiation was 6.7 [2.3; 12.0] years old (range: 4 days to 22 years old), and was statistically different between subgroups (Table 2). Children in the CAH group were significantly younger, and children in the multiple disabilities group significantly older than children in the other groups ( $p < .001$ ). Median [IQR] duration of NIV/CPAP treatment at the time of the survey was 1.9 [0.6; 3.8] years. It was significantly longer for patients with



CNS tumors and CAH compared to the other groups ( $p < .01$ ). Seventy-five percent of the patients were treated with NIV, 23% with CPAP (with only three patients in auto-set CPAP and 2% with adaptive servo-ventilation. NIV was predominantly used in all subgroups, especially in non-tumor spinal cord injury and CAH (89% and 88%, respectively).

**TABLE 3** Investigations performed before NIV/CPAP initiation and initiation criteria.

Investigations, n (%)	Total population (n = 182)	Nontumor spinal cord injury (n = 35)	CNS tumors (n = 22)	Multiple disabilities (n = 63)	Central alveolar hypoventilation (n = 26)	Others CNS diseases (n = 36)
<b>Investigations performed before NIV/CPAP initiation</b>						
Nocturnal SpO <sub>2</sub> + PtcCO <sub>2</sub> recording	53 (29%)	11 (31%)	4 (18%)	24 (38%)	5 (19%)	9 (25%)
PG/PSG + nocturnal SpO <sub>2</sub> + PtcCO <sub>2</sub> recording	61 (34%)	13 (37%)	8 (36%)	19 (30%)	9 (35%)	12 (33%)
PG/PSG	35 (19%)	3 (9%)	8 (36%)	7 (11%)	7 (27%)	10 (27%)
Nocturnal SpO <sub>2</sub> recording (alone)	1 (1%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)
Spirometry	2 (1%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)
No investigation	20 (11%)	5 (14%)	1 (5%)	8 (13%)	4 (15%)	2 (6%)
Missing data	10 (5%)	2 (6%)	1 (5%)	4 (6%)	1 (4%)	2 (6%)
<b>NIV/CPAP initiation criteria</b>						
Nocturnal SpO <sub>2</sub> + PtcCO <sub>2</sub> recording	55 (30%)	11 (31%)	3 (14%)	25 (40%)	8 (31%)	8 (22%)
AHI	42 (23%)	5 (14%)	8 (36%)	10 (16%)	7 (27%)	12 (33%)
AHI + nocturnal SpO <sub>2</sub> /PtcCO <sub>2</sub> recording	42 (23%)	8 (23%)	7 (32%)	11 (17%)	6 (23%)	10 (28%)
Nocturnal SpO <sub>2</sub> recording (alone)	3 (2%)	0 (0%)	0 (0%)	3 (5%)	0 (0%)	0 (0%)
Nocturnal PtcCO <sub>2</sub> recording (alone)	3 (2%)	1 (3%)	1 (5%)	0 (0%)	0 (0%)	1 (3%)
AHI + nocturnal SpO <sub>2</sub> recording	3 (2%)	1 (3%)	1 (4.5%)	1 (2%)	0 (0%)	0 (0%)
Total lung capacity	2 (1%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Clinical criteria	18 (10%)	6 (17%)	1 (5%)	7 (11%)	2 (8%)	2 (6%)
IV weaning	9 (5%)	4 (11%)	1 (5%)	2 (3%)	2 (8%)	0 (0%)
ICU initiation	7 (4%)	1 (3%)	0 (0%)	4 (6%)	0 (0%)	2 (6%)
Others	2 (1%)	1 (3%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)
No criteria	4 (2%)	0 (0%)	0 (0%)	2 (3%)	2 (7.5%)	0 (0%)
Missing data	10 (5%)	2 (6%)	1 (5%)	4 (6%)	1 (4%)	2 (6%)

Abbreviations: AHI, apnea-hypopnea index; CNS, central nervous system; CPAP, continuous positive airway pressure; ICU, intensive care unit; IV, invasive ventilation; NIV, noninvasive ventilation; PG, respiratory polygraphy; PSG, polysomnography; PtcCO<sub>2</sub>, transcutaneous carbon dioxide pressure; SpO<sub>2</sub>, pulse oximetry.

Investigations performed before NIV/CPAP initiations are presented in Table 3. Nocturnal pulse oximetry (SpO<sub>2</sub>) and transcutaneous carbon dioxide pressure (PtcCO<sub>2</sub>), alone or coupled with Poly (somno)graphy (P(S)G), were the most frequently performed investigations (in 29% and 34% of the patients, respectively). In 20 (11%) children, no investigation was performed. Nocturnal gas exchanges were the most common investigation in patients with multiple disabilities.

NIV/CPAP initiation was based on nocturnal SpO<sub>2</sub> and/or PtcCO<sub>2</sub> in 34% of the patients, apnea-hypopnea index (AHI) in 23% of the patients, and the association of AHI and nocturnal gas exchange recordings in 25% of the patients. NIV/CPAP initiation was performed on an acute setting (clinical criteria) in 10% of the patients, mainly in patients with non-tumor spinal cord injury and multiple disabilities (Table 3).

**TABLE 4** NIV/CPAP adherence and equipment.

	Total population (n = 182)	Nontumor spinal cord injury (n = 35)	CNS tumors (n = 22)	Multiple disabilities (n = 63)	Central alveolar hypoventilation (n = 26)	Others CNS diseases (n = 36)
<b>NIV/CPAP adherence</b>						
Adherence (hours/ night)	8 [6;10]	9 [8;10]	8 [8;9]	7 [4;9.5]	10 [8;10]	8 [6;8.3]
<4 h/day (n, %)	22 (12%)	1 (3%)	2 (9%)	11 (17%)	1 (4%)	7 (19%)
≥16 h/day (n, %)	2 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)	1 (3%)
Missing data (n, %)	15 (8%)	4 (11%)	2 (9%)	8 (13%)	1 (4%)	0 (0%)
<b>Type of devices</b>						
Standard (n, %)	40 (22%)	4 (11%)	9 (41%)	14 (22%)	3 (12%)	10 (28%)
Intermediate (n, %)	67 (37%)	19 (54%)	6 (27%)	28 (44%)	4 (15%)	10 (28%)
Life support (n, %)	70 (38%)	11 (31%)	7 (32%)	18 (29%)	19 (73%)	15 (42%)
Missing data (n, %)	5 (3%)	1 (3%)	0 (0%)	3 (5%)	0 (0%)	1 (3%)
<b>Interfaces</b>						
Nasal (n, %)	128 (70%)	26 (74%)	10 (45%)	46 (73%)	16 (62%)	30 (83%)
Nasobuccal (n, %)	38 (21%)	7 (20%)	8 (36%)	12 (19%)	6 (23%)	5 (14%)
Nasal prongs (n, %)	5 (3%)	1 (3%)	1 (5%)	1 (2%)	1 (4%)	1 (3%)
Total face (n, %)	2 (1%)	0 (0%)	1 (5%)	1 (2%)	0 (0%)	0 (0%)
Missing data (n, %)	9 (5%)	1 (3%)	2 (9%)	3 (5%)	3 (12%)	0 (0%)
<b>NIV settings</b>						
IPAP max (cmH <sub>2</sub> O)	13 [12;16.5]	13 [12;18]	14.5 [12;21.5]	13.5 [12;16]	14 [12.7;18]	12 [10;14]
EPAP max (cmH <sub>2</sub> O)	5 [4; 6]	5 [4; 6]	5.5 [4.3; 6.8]	5 [4; 6]	4 [4; 5]	5 [4; 6]
Pressure support (cmH <sub>2</sub> O)	8 [6; 11.8]	8 [6; 11]	8 [6.3; 15]	7 [6.0; 11.5]	10 [8.0; 13.3]	7 [5; 8]
BUR (breaths/min)	20 [16; 24.5]	18 [15; 20]	18 [16.5; 22]	19 [16; 20]	22 [20; 25]	20 [15.8; 25]
<b>CPAP settings</b>						
CPAP (cmH <sub>2</sub> O)	7 [6; 8]	7 [6.8; 6.8]	7 [6; 7]	7 [7; 9]	6	7 [6; 7.8]

Note: Data are given as median [Q1; Q3].

Abbreviations: BUR, back up rate; CNS, central nervous system; CPAP, continuous positive airway pressure; EPAP, expiratory airway pressure; IPAP, inspiratory airway pressure; NIV, noninvasive ventilation.

NIV adherence and equipment are presented in Table 4. Median NIV/CPAP adherence was good with a median use of 8.0 h per night. Overall, 22 children (12%) used the ventilatory support device less than 4 h/day, with higher rates of nonadherence in the multiple disabilities and other CNS diseases groups (17% and 19%, respectively). A use of NIV ≥16 h/day was exceptional. Intermediate and life support devices were the most frequently used (37% and 38% of the children, respectively). Seventy three percent of patients with central alveolar hypoventilation were prescribed life support devices. Standard devices were used in 41% of children with CNS tumors.

Nasal mask was the most commonly used interface (70% of the total population), followed by nasobuccal interface (21% of the total population). Settings are described in Table 4.

Airway clearance techniques were used by only 56 (31%) patients, more frequently by patients of the non-tumor spinal cord injury, multiple disabilities or others CNS diseases subgroups (Table 5). Among children being prescribed airway clearance devices, the majority of

the patients (73%) had one device: intermittent positive pressure breathing (IPPB, 45%), mechanical in-exsufflator (MI-E, 25%) or intrapulmonary percussive ventilation (IPV, 4%).

## 4 | DISCUSSION

This study provides a unique national overview of the use of longterm ventilatory support in children with CNS disorders. Children with multiple disabilities composed the largest subgroup with 63 (35%) patients. NIV was the most frequent ventilatory mode, in 75% of children, and the main initiation criteria for CPAP/NIV was nocturnal gas exchange recordings, alone or coupled P(S)G (63%).

Treatment adherence was considered good (>4 h/day) in almost 90% of patients. The use of airway clearance devices remained relatively low, considering that only 31% of the overall population and 43% of children with multiple disabilities were prescribed at least one device. Long term NIV/CPAP has greatly increased in children during the past 20 years, with a concomitant decrease of invasive ventilation. [2,18–23](#) This evolution is explained by an increased survival of children with complex diseases including those with CNS disorders, development of home care, improvement of devices that are now better adapted to children, better screening of sleep disordered breathing and finally development of pediatric centers with an expertise in long term ventilatory support.[24](#)

The number of children treated with long-term noninvasive ventilatory support in France has increased from 102 to 1447 between 2003 and 2019.[18](#) During this period, the number of children with CNS disorders treated by NIV/CPAP has been multiplied by 16, from 11 to 182 children.[18](#) Similar trends have been observed in Canada, Italy, and Spain.[23,25–27](#)

Nocturnal gas exchange recordings were the main investigation performed before NIV/CPAP initiation. In 29% of children, it was the sole investigation. It was associated with a P(S)G in 34% of patients. Similarly, NIV/CPAP initiation was decided on the presence of nocturnal hypoventilation (30% of patients), a high AHI (23%) or both (23%). No investigation was performed in 11% of patients, NIV/CPAP was initiated in an acute setting in 10% of children, after weaning of invasive ventilation or in the intensive care unit following an acute respiratory failure. These results differ from those of a previous study on NIV in complex obstructive sleep apnea syndrome (OSAS), including patients with CNS disorders, which reported that 51% of patients did not have any investigation before starting NIV and that in 38% of patients, NIV was initiated in an acute setting.[28](#) This discrepancy illustrates the evolution of the respiratory management of patients with CNS disorders, possibly explained by the increased availability of nocturnal gas exchange recordings and P(S)G, and the improvement in the screening of sleep disordered breathing.[28](#)

Except in patients with CCHS and CNS tumors for whom PSG is the gold standard for screening of sleep-disordered breathing, there is a lack of recommendations on the investigations that should be performed before NIV/CPAP initiation, especially in the multiple disabilities group. Recent French national recommendations for children with multiple disabilities recommended nocturnal SpO<sub>2</sub> or PtcCO<sub>2</sub> recordings, and when pathological or in case of suspicion of sleep-disordered breathing, polysomnographic recordings.[1](#) These recommendations have to be put into perspective considering the difficulty of performing complex sleep recordings in patients with neurodisabilities.

NIV was predominantly used in our population, which is concordant with the comorbidities of these patients, which are recognized risk factors for nocturnal hypoventilation (scoliosis, ineffective cough, and repeated lower respiratory tract infections).<sup>1,29</sup> Median inspiratory and expiratory positive airway pressures were 13 and 5 cmH<sub>2</sub>O, respectively, with patients with CNS tumors requiring higher pressures. This is close to what has been described in the global French pediatric population using ventilator support, and to what has been reported in the European Respiratory Society Statement on pediatric long-term noninvasive respiratory support.<sup>18,29</sup> Nasal mask was the most commonly used interface (70%), followed by nasobuccal mask (21%). This is similar to what has been previously described.<sup>18,30</sup> In patients with CNS disorders, the use of nasobuccal masks must be very careful, considering the risk of gastro-oesophageal reflux and inhalation in this population. Nasal masks limit this risk but with the risk of unintentional leaks and suboptimal control of sleep-disordered breathing.<sup>31</sup>

The overall median treatment use in our study population was good, with a median use of 8 [6;10] hours/night. Adherence was considered as poor (<4 h/day) in only 12% of the population, but in 17% of children with multiple disabilities and 19% of children with other CNS diseases. These last results are similar to a study by Girbal et al.<sup>28</sup> who reported a poor adherence in 22% of patients with CNS disorders presenting with complex OSAS. Previous studies have suggested that neurocognitive impairment may be associated with a poor adherence, but our results do not corroborate these observations.<sup>32–35</sup>

Only 31% of children were prescribed at least one airway clearance technique, with half of the patients of the non-tumor spinal cord injury group and 43% in the multiple disabilities group using at least one device. Intermittent positive pressure breathing was the main prescribed technique (19%), while mechanical in-exsufflation and intrapulmonary percussive ventilation were prescribed in 17% and 6% of children, respectively. This was significantly lower than what has been reported in children with neuromuscular diseases, of whom 66% were prescribed at least one airway clearance technique.<sup>36</sup> This is a surprising result considering the common substrate for chronic respiratory insufficiency in these two groups: decreased cough efficiency, increased secretions and scoliosis.<sup>1</sup> This result is also in contradiction with national recommendations on the respiratory management of children with multiple disabilities.<sup>1</sup> It would be interesting to analyze the management differences in each center to standardize the respiratory care and secretion management in these different groups of patients.

This study has several limitations. The main one is the absence of data on the effect of NIV/CPAP on health outcomes such as quality of life, the necessity of hospitalizations and the frequency of respiratory exacerbations. It does not present precise data on the results of the different investigations, especially on AHI, SpO<sub>2</sub>, PtcCO<sub>2</sub> or blood gas findings. It would also be interesting to report the proportion of patients with multiple disabilities that were screened for sleep-disordered breathing, and the number of patients eventually treated with NIV/CPAP among them. Finally, there is insufficient information on associated comorbidities such as scoliosis, obesity, ENT associated disorders and epilepsy, which could affect treatment tolerance and evolution.

The number of missing data remained relatively low, mostly under 5%, although data in the central alveolar hypoventilation subgroup are incomplete, considering that the number of included patients with CCHS does not match the number of patients followed in the French reference center. Finally, information on NIV/CPAP failure was not available in this study, which constitutes a major problem in this challenging population.

## **5 | CONCLUSION**

This national multicenter study describes one of the largest populations of children with CNS disorders treated with long term NIV/CPAP, with a total of 182 patients. It reflects the development of NIV/CPAP in the pediatric population, especially in this subgroup of patients with complex and challenging pathologies. It also showed that airway clearance techniques were used in only a small number of children, even in the subgroup of children with multiple disabilities, where it could potentially be an effective means of preventing the progression towards hypoventilation and chronic respiratory insufficiency.

This highlights the need for studies on patient reported outcome measures (sleep quality, quality of life) and on clinical efficiency (number of hospitalizations and respiratory exacerbations) of long term NIV/CPAP, and the necessity to standardize sleep disordered breathing screening and patient's management. Further research is required to offer additional insights into the initiation criteria for ventilatory support in this population, including parameters such as SpO<sub>2</sub>, PtcCO<sub>2</sub>, AHI, and to establish efficient management protocols and therapeutic education strategies to promote treatment adherence.

### **AUTHOR CONTRIBUTIONS**

This survey is a collaborative work of all the members of the French pediatric NIV national network. Marion Carrara and Jessica Taytard: analyzed the data, and wrote the final draft of the manuscript. L. Brigitte Fauroux: designed the study. All the co-authors included the patients, carefully read the manuscript and contributed with their comments and suggestions to the final version of the manuscript. The final version was approved by all the co-authors.

### **ACKNOWLEDGMENTS**

The authors thank the patients and families for their participation in this study.

### **CONFLICT OF INTEREST STATEMENT**

The authors declare no conflicts of interest.

### **DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

This study obtained the ethics committee approval (Comité d'Ethique de Necker Enfants malades, CENEM, No. CENEM19-5-BF) on March the 7th 2019, and all patients aged >6 years and parents gave their informed consent.

## REFERENCES

1. DéfiScience, Filière de Santé des Maladies Rares du Neuros-développement. Protocole National de Diagnostic et de Soins (PNDS) Générique Polyhandicap. 2020at; [https://www.has-sante.fr/upload/application/pdf/2020-05/11\\_mai\\_2020\\_text...](https://www.has-sante.fr/upload/application/pdf/2020-05/11_mai_2020_text...)
2. Amin R, Sayal P, Syed F, Chaves A, Moraes TJ, MacLusky I. Pediatric long-term home mechanical ventilation: twenty years of follow-up from one Canadian center. *Pediatr Pulmonol.* 2014;49:816-824.
3. Beh SC, Greenberg BM, Frohman T, Frohman EM. Transverse myelitis. *Neurol Clin.* 2013;31:79-138.
4. Erkkinen MG, Berkowitz AL. A clinical approach to diagnosing encephalopathy. *Am J Med.* 2019;132:1142-1147.
5. Eisenberg A, Hobart-Porter L, Jambhekar S, et al. Sleep related breathing disorders in the spina bifida population ages 1-20 years: a retrospective study in Arkansas. *J Pediatr Rehabil Med.* 2022;15:581-586.
6. Khatwa U, Ramgopal S, Mylavarapu A, et al. MRI findings and sleep apnea in children with Chiari I malformation. *Pediatr Neurol.* 2013;48:299-307.
7. Ramirez J-M, Karlen-Amarante M, Wang J-DJ, Huff A, Burgraff N. Breathing disturbances in Rett syndrome. *Handb Clin Neurol.* 2022;189:139-151.
8. Bulian A, Couloigner V, Belhous K, Luscan R, Khirani S, Fauroux B. Sleep-disordered breathing in pediatric neurofibromatosis type 1. *Am J Med Genet, Part A.* 2022;188:1964-1971.
9. Amaddeo A, De Sanctis L, Arroyo JO, Khirani S, Bahi-Buisson N, Fauroux B. Polysomnographic findings in Rett syndrome. *Eur J Paediatr Neurol.* 2019;23:214-221.
10. Leoncini S, Signorini C, Boasiako L, et al. Breathing abnormalities during sleep and wakefulness in Rett syndrome: clinical relevance and paradoxical relationship with circulating pro-oxidant markers. *Front Neurol.* 2022;13:833239.
11. Sankari A, Bascom A, Oomman S, Badr MS. Sleep disordered breathing in chronic spinal cord injury. *J Clin Sleep Med.* 2014;10:65-72.
12. Ghirardo S, Amaddeo A, Griffon L, Khirani S, Fauroux B. Central apnea and periodic breathing in children with underlying conditions. *J Sleep Res.* 2021;30:e13388.
13. Rosen G, Brand SR. Sleep in children with cancer: case review of 70 children evaluated in a comprehensive pediatric sleep center. *Supp Care Cancer.* 2011;19:985-994.
14. Sforza E, Colamaria V, Lugaresi E. Neurofibromatosis associated with central alveolar hypoventilation syndrome during sleep. *Acta Paediatr (Stockholm).* 1994;83:794-796.
15. Amaddeo A, Frapin A, Fauroux B. Long-term non-invasive ventilation in children. *Lancet Respir Med.* 2016;4:999-1008.

16. Juzeau D, Cachera I, Vallée L. [Epidemiologic study of multihandicapped children in the north of France]. *Arch Pediatr*. 1999;6:832-836.
17. Rumeau-Rouquette C, du Mazaubrun C, Cans C, Grandjean H. [Definition and prevalence of school-age multi-handicaps]. *Arch Pediatr*. 1998;5:739-744.
18. Fauroux B, Khirani S, Amaddeo A, et al. Paediatric long term continuous positive airway pressure and noninvasive ventilation in France: a cross-sectional study. *Respir Med*. 2021;181:106388.
19. Wallis C, Paton JY, Beaton S, Jardine E. Children on long-term ventilatory support: 10 years of progress. *Arch Dis Child*. 2011;96:998-1002.
20. McDougall CM, Adderley RJ, Wensley DF, Seear MD. Long-term ventilation in children: longitudinal trends and outcomes. *Arch Dis Child*. 2013;98:660-665.
21. Racca F, Bonati M, Del Sorbo L, et al. Invasive and non-invasive long-term mechanical ventilation in Italian children. *Minerva Anestesiol*. 2011;77:892-901.
22. Goodwin S, Smith H, Langton Hewer S, et al. Increasing prevalence of domiciliary ventilation: changes in service demand and provision in the South West of the UK. *Eur J Pediatr*. 2011;170:1187-1192.
23. Castro-Codesal ML, Dehaan K, Bedi PK, et al. Longitudinal changes in clinical characteristics and outcomes for children using long-term non-invasive ventilation. *PLoS One*. 2018;13:e0192111.
24. Gulla KM, Sahoo T, Sachdev A. Technology-dependent children. *Int J Pediatr Adolesc Med*. 2020;7:64-69.
25. González Cortés R, Bustinza Arriortua A, Pons Ódena M, et al. [Domiciliary mechanical ventilation in children: a Spanish multicentre study]. *An Pediatr Barc Spain*. 2013;2003:227-233.
26. Bedi PK, DeHaan K, MacLean JE, Castro-Codesal ML. Predictors of longitudinal outcomes for children using long-term noninvasive ventilation. *Pediatr Pulmonol*. 2021;56:1173-1181.
27. Pavone M, Verrillo E, Onofri A, Caggiano S, Chiarini Testa MB, Cutrera R. Characteristics and outcomes in children on long-term mechanical ventilation: the experience of a pediatric tertiary center in Rome. *Ital J Pediatr*. 2020;46:12.
28. Girbal IC, Gonçalves C, Nunes T, et al. Non-invasive ventilation in complex obstructive sleep apnea-a 15-year experience of a pediatric tertiary center. *Rev Port Pneumol*. 2014;20:146-151.
29. Fauroux B, Abel F, Amaddeo A, et al. ERS statement on paediatric long-term noninvasive respiratory support. *Eur Respir J*. 2022;59:2101404.
30. Ramirez A, Delord V, Khirani S, et al. Interfaces for long-term noninvasive positive pressure ventilation in children. *Intensive Care Med*. 2012;38:655-662.
31. Castro-Codesal ML, Olmstead DL, MacLean JE. Mask interfaces for home non-invasive ventilation in infants and children. *Paediatr Respir Rev*. 2019;32:66-72.
32. Blinder H, Momoli F, Holland SH, Blinder A, Radhakrishnan D, Katz SL. Clinical predictors of nonadherence to positive airway pressure therapy in children: a retrospective cohort study. *J Clin Sleep Med*. 2021;17:1183-1192.
33. Blinder H, Momoli F, Bokhaut J, et al. Predictors of adherence to positive airway pressure therapy in children: a systematic review and meta-analysis. *Sleep Med*. 2020;69:19-33.
34. Kang EK, Xanthopoulos MS, Kim JY, et al. Adherence to positive airway pressure for the treatment of obstructive sleep apnea in children with developmental disabilities. *J Clin Sleep Med*. 2019;15:915-921.
35. Hawkins SMM, Jensen EL, Simon SL, Friedman NR. Correlates of pediatric CPAP adherence. *J Clin Sleep Med*. 2016;12:879-884.

36. Allaer L, Khirani S, Griffon L, et al. Long term noninvasive ventilation and continuous positive airway pressure in children with neuromuscular diseases in France. *Neuromuscular Disord.* 2022;32:886-892.