Clinical Investigations

Respiration

Respiration 2010;80:379–386
DOI: 10.1159/000254378

Received: July 2, 2009
Accepted after revision: August 27, 2009
Published online: October 29, 2009

Mouth and Nasal Inspiratory Pressure: Learning Effect and Reproducibility in Healthy Adults

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Key Words
Learning effect · Respiratory function tests · Respiratory muscle strength · Results, reproducibility · Volitional tests

Abstract
Background: Inspiratory muscle strength measurements have become a cornerstone in monitoring neuromuscular disorders. Usually, sniff nasal inspiratory pressure (SNIP) and maximal inspiratory pressure (MIP) are performed. To our knowledge the session-to-session learning effect has rarely been evaluated for MIP performance and has never been done for SNIP performance. ***Objectives:*** We hypothesized that the sniff manoeuvre was natural and did not need to be learned, whereas the Muller manoeuvre, used for MIP measurement, was an isometric contraction which needed to be learned because it is rarely performed in real life conditions. This hypothesis suggests that from the first session and continuing through a subsequent one, the maximal SNIP value and the number of sniff trials necessary to attain it are more reproducible than the maximal MIP value and the number of Muller manoeuvre trials necessary to attain it. ***Methods:*** Seventy-one healthy subjects were included. SNIP and MIP manoeuvres were repeated 12 and 6 times, respectively, per week during 2 sessions a week apart. ***Results:*** We observed a session effect on MIP but not on SNIP. Maximal value for MIP was higher during the second session, whereas SNIP maximal value did not increase during the second session. The number of trials needed to obtain the maximal value for MIP was lower during the second session whereas it was not different for SNIP. ***Conclusions:*** SNIP is less sensitive to a learning effect than is MIP. It requires only a routine warm-up. We suggest that SNIP is preferable to MIP for repeated measurement of inspiratory muscle performance.

Introduction

Measurement of respiratory muscle strength is clinically useful in the assessment and the follow-up of patients with neuromuscular diseases [1–5]. Conventional non-invasive assessment of inspiratory muscle strength is performed using mouth-pressure measurements obtained during maximal inspiratory effort against an occlusion for at least 1 s [6]. As this static manoeuvre is difficult to perform, the results may vary widely and low values may not only reflect a true inspiratory muscle

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weakness, but also a lack of motivation and/or poor coordination. Sniffing is a more natural manoeuvre and is easier to perform than static efforts for many patients. Therefore, sniff nasal inspiratory pressure (SNIP) measurement has been proposed as an alternative to maximal inspiratory pressure (MIP) [1, 6]. However, sniff nasal pressure results in similar over-diagnosis of inspiratory muscle weakness as MIP [3]. Finally, combining SNIP and MIP manoeuvres drastically reduces the over-diagnosis of weakness compared to either manoeuvre alone [3].

Like spirometry, SNIP and MIP manoeuvres have been considered as useful tools for monitoring the evolution of a neuromuscular disorder [1, 4, 5, 7–13]. The number of sniffs and MIP that are necessary to obtain a maximal value has been evaluated in previous studies [14, 15]. Data concerning the follow-up are conflicting, nevertheless the use of sniff nasal inspiratory pressure measurement alone has been suggested for monitoring patients with amyotrophic lateral sclerosis [4, 16]. In the 2 most common chronic neuromuscular diseases, Duchenne muscular dystrophy and Steinert myotonic dystrophy, we have highlighted that – under certain conditions – it could be appropriate to use just 1 test for follow-up [5].

Therefore, in order to improve the follow-up it appears important to know if these tests are sensitive to a learning effect over time. The within-session learning effect and reproducibility over time has been extensively evaluated for both MIP and SNIP manoeuvres [4, 12–14, 17–22], but to our knowledge the session-to-session learning effect has rarely been evaluated for MIP performance [23, 24] and has never been done for SNIP performance.

We hypothesized that the sniff manoeuvre was natural and did not need to be learned, whereas the Muller manoeuvre used for MIP measurement was an isometric contraction of the inspiratory muscles which needed to be learned because it is rarely performed in real life. In practice, this hypothesis suggests that from the first session and continuing through a subsequent one, the maximal SNIP value and the number of sniff trials necessary to attain it are more reproducible than the maximal MIP value and the number of Muller manoeuvre trials necessary to attain it.

To test this hypothesis, we compared 2 sessions of SNIP manoeuvres and MIP manoeuvres separated by 1 week. Because the inspiratory muscle function cannot be considered as stable in the neuromuscular-disease population and because most of these patients have learned these manoeuvres before, we decided to answer this question by studying a healthy/untrained population.

Methods

Subjects and Protocol

Data was obtained from medical students during practical teaching sessions dedicated to respiratory function testing. The protocol was approved by the regional ethical committee (Comité de Protection des Personnes Nord Ouest III).

Before inclusion, the subjects were offered a barometric whole body plethysmography and spirometry (CompactLab Jaeger, Wuerzburg, Germany) in order to eliminate abnormal pulmonary function. For each manoeuvre 5 trials were carried out in order to evaluate the within-subject coefficient of variation for each parameter measured. The subjects were aware of respiratory physiology but had never performed mouth MIP or SNIP measurements. As the measurements were taken during a teaching session, the students had to come to the laboratory in pairs. One student in the pair then underwent the series of measurements of MIP followed by SNIP measurements. The other student in the pair performed the measurements in reverse order (SNIP then MIP). A week later, the same pair of students came to the laboratory to repeat the measurements of MIP and SNIP with the same procedure. Following this scheme, the same number of students began with MIP or SNIP. All the measurements of MIP and SNIP were done by the same person. The same flanged mouthpiece was used for plethysmography, spirometry and maximal pressure measurements as this piece of equipment is recommended for MIP measurements [6].

Mouth and Sniff Nasal Inspiratory Pressure

MIP and SNIP were measured at functional residual capacity (FRC) in a sitting position, with no visual feedback, with a differential pressure transducer (Validyne P300, Validyne Corporation, Northridge, Calif., USA), range ± 200 cm H_2O, connected to a Gould amplifier (20-4615-50) and a Gould TA11 thermal paper recorder. The transducer was calibrated at each session with a 140-cm water column and the acquisition frequency of the recorder was set to 1 kHz.

For MIP measurements, the subjects wore a nose clip and breathed through a flanged mouthpiece connected to a stopcock and a No. 1 Fleisch pneumotachograph. The flow signal was measured with a Validyne DP45 differential pressure transducer connected to a Gould amplifier and integrated to give a tidal volume recorded on the thermal paper recorder at 1 $cm \cdot s^{-1}$. Pressure was measured through a side connector. Another side connector (1 mm internal diameter) served as a leak to prevent participation from orofacial muscles. A piece of small plastic tubing was plugged into this connector and its length was adjusted so that the flow of the leak was approximately 100 $ml \cdot s^{-1}$ at a pressure of 100 cm H_2O. This leak was considered sufficient to prevent utilization of the facial muscles while maintaining the lung volume close to the FRC during the measurement (under normal MIP the mouth gas volume would have increased by 100 ml in 1 s making it impossible for the subject to maintain the maximal pressure).

After the manoeuvre was carefully explained, the stopcock was closed at the end expiratory level as judged by the integrated flow signal and the subject was instructed to exert maximal inspiratory effort for approximately 2 or 3 s. Unless accidentally interrupted or in the case of obvious failure, the manoeuvre was repeated only 6 consecutive times with a 30-s pause between trials. The number of trials was chosen as twice the minimal number

recommended by the American Thoracic Society and the European Thoracic Society (ATS/ERS) [6].

MIP was measured as the maximal mean pressure held for 1 s. It was determined by an averaging on the recorder tracing as depicted in the ATS/ERS statement on respiratory muscle testing [6].

For SNIP measurements we used a dedicated balloon-type catheter (ref A26U, Marquat génie biomédical, Boissy-Saint-Léger, France). The catheter, 50-cm long, is made of polyvinyl chloride. The balloon surrounds the catheter extremity, while its lumen remains outside the balloon. It was possible to wedge this extremity into the nostril using the same principle as a Swan-Ganz catheter wedged in the pulmonary circulation. The other catheter extremity was connected to the differential pressure transducer. The frequency response of the whole measuring system, including the catheter, the pressure transducer and the recorder was tested in 2 ways. The tip of the catheter was placed into a 60-ml plastic syringe and sealed with silicone paste inside the tip of the syringe. A hole was drilled in the body of the syringe. A square pressure wave was obtained by pulling the piston while the hole was blocked off with the thumb and then abruptly opened ('pop-test'), allowing measurement of the natural frequency and damping coefficient. The frequency response was also studied by applying a sinusoidal pressure around the tip of the catheter or directly to the transducer. The pressure was generated by the loudspeaker of a piece of lung-function testing equipment made to deliver forced oscillations (Pulmosfor, SEFAM, Nancy, France). The amplitude ratio of the pressure measured directly by the transducer over the pressure measured through the catheter and connecting tubing was calculated every 2 Hz at frequencies between 2 and 32 Hz (the maximum frequency of the lung function measurement system). The natural frequency of the system was approximately 100 Hz and no damping was observed, up to the limit of our pressure generator (32 Hz). These characteristics ensured that the sniff pressure was correctly measured. Before SNIP measurement, the subject was asked to blow their nose. The permeability of both nostrils was clinically verified one by one during sniffing. Any subjects reporting nasal congestion or cold symptoms at either session were excluded. The catheter was placed into the right nostril in such a way that the balloon slightly overflowed the nostril when inflated. Complete wedging of the nostril was verified by asking the subject to blow through their nose while the left nostril was manually blocked. Permeability of the left nostril was verified while the balloon was inflated. The balloon was kept inflated with a stopcock. After the manoeuvre was explained, the subject was asked to produce 12 consecutive maximal, brief, sharp sniffs through the open nostril, starting from the end expiratory level, with a 30-s pause between trials. The number of trials chosen was above the minimum number of trials recommended by ATS/ERS [6]. Because the sniffs were done with the mouth shut, the end expiratory level was verified clinically. All the trials with a sharp signal were kept, i.e. all signals with smooth upstroke and a time to peak less than 400 ms were retained [1], excluding plateau, biphasic aspect and long duration sniff efforts.

Statistical Analysis

Demographic characteristics and all respiratory function measurements were described using mean ± standard deviation (SD).

Within-subject coefficients of variation for vital capacity (VC), forced vital capacity (FVC), thoracic gas volume at end expiratory level (TGV), total lung capacity (TLC), forced expiratory volume in 1 s (FEV_1), MIP and SNIP were calculated as the ratio of the SD over the mean.

Because the rank of the trial that gave the maximal value for MIP or SNIP was not distributed normally, a Wilcoxon test was used in order to compare the week effect on this parameter. In contrast, the MIP and SNIP values were normally distributed, therefore parametric tests were performed. Peak value comparison between weeks was performed by a paired t test. For the values which were repeated within the weeks, the week effect and the trial effect were evaluated using a 2-factor analysis of variance (ANOVA) for repeated measurements (trial effect and week effect). When an interaction existed between the two factors, a 1-way ANOVA for repeated measurements was repeated independently for the 2 weeks.

Values of $p < 0.05$ were considered statistically significant. Statistical tests were run using the StatView 5 package (SAS Institute, Grenoble, France).

Results

Study Population

Ninety-two healthy medical students, with no history of neurological or muscle disease, gave their informed consent and served as volunteers. However, 1 student did not provide a medical history, 2 students did not show up at the second session and SNIP measurement was not possible in 1 patient because her nostrils were too narrow for insertion of the plugging system into the nasal cavity. Among the 89 remaining students, 18 presented nasal congestion at either session and were not included because sniffing might have been difficult due to upper airway obstruction [25]. None of them declared active endurance training.

Table 1 reports the physical characteristics of the 71 remaining subjects included in the study. At the time of inclusion in the study, their mean age was 20.9 ± 0.9 for males and 20.7 ± 0.9 for females. All the subjects had a VC, a TLC and a FEV_1 greater than 88% of predicted values. In some subjects, the sniff pressure signal showed a small plateau in the first trials, probably because the tip of the catheter stuck onto the mucous nasal membrane. Replacement of the catheter always allowed us to record sharp signals. Some subjects complained of slight ear pain during SNIP measurements. For one of them the measurement session was ended because of this sensation. The catheter itself was well-tolerated with no need to be re-inflated or maintained during the procedure.

Table 1. Physical characteristics of the subjects

	Males (n =29)			Females (n = 42)		
	min	max	mean ± SD	min	max	mean ± SD
Age, years	19.3	22.3	20.9 ± 0.9	18.8	24.3	20.7 ± 0.9
Weight, kg	56	85	71 ± 7	41	75	56 ± 7
Height, cm	170	191	178 ± 5	155	183	167 ± 6
BMI	18	27	22 ± 2	15	29	20 ± 3
VC, % ERS predicted	89	128	107 ± 9	85	140	105 ± 11
TLC, % ERS predicted	88	126	104 ± 9	83	128	104 ± 10
FEV_1, % ERS predicted	98	139	116 ± 11	86	151	108 ± 12

All subjects were healthy and had no nasal obstruction.
% ERS predicted = Percent of end respiratory stage predicted value.

Table 2. Coefficients of variation for the first week (n = 71)

	Coefficients of variation, %		
	min	max	mean ± SD
VC	0.5	12.0	2.2 ± 1.8
TGV	2.0	18.4	5.3 ± 3.2
TLC	0.4	11.1	2.4 ± 1.6
FEV_1	0.2	9.0	2.5 ± 1.9
$MIP_{(1–6)}$	2.3	36.2	11.4 ± 7.8
$SNIP_{(1–12)}$	4.9	20.0	10.0 ± 3.4

$MIP_{(1–6)}$ = Maximal (hold for 1 s) inspiratory pressure at FRC level (all 6 trials); $SNIP_{(1–12)}$ = sniff nasal inspiratory pressure at FRC level (all 12 trials).

Within-Subject Variability

Within-subject coefficients of variation for VC, FEV_1 and TLC were not different from those observed in previous studies (respectively 2.2 ± 1.8%, 2.5 ± 1.9% and 2.4 ± 1.6%) [26]. For all parameters of spirometry, the coefficients of variation were similar for males and females (not shown; table 2).

Within-subject coefficients of variation for MIP and SNIP were in agreement with previous studies [18, 27].

Comparison of Maximal Inspiratory Pressures

The best MIP was significantly higher during the second week (97 ± 28 vs. 101 ± 30, p = 0.006, paired t test), while the best SNIP did not differ from the first to the second week (115 ± 28 vs. 114 ± 26, p = 0.76, paired t test).

Evolution of Pressure Measurement during the Consecutive Trials

Mouth Inspiratory Pressure

The mean trial number during which the maximal value for MIP was obtained was 4.5 ± 1.7 on the first session and 3.4 ± 1.9 for the second (p = 0.0008, Wilcoxon). Fig. 1a and b show the distribution of the rank of trial giving the best value of mouth inspiratory pressure during each session.

When a 2-way ANOVA with repeated measurements was performed, a week effect and a trial effect was observed (p = 0.0008 and $p < 0.0001$ respectively; fig. 2). A significant interaction was observed between these 2 factors ($p < 0.0001$). Accordingly, using a 1-way ANOVA (trial effect) with repeated measurements, we noted in the first week's session a trial effect ($p < 0.0001$), whereas during the second week's session no trial effect was observed (p = 0.65).

Sniff Nasal Inspiratory Pressure

Fig. 1c and d show the distribution of the rank of the maximal trial. The mean trial number during which the maximal value of SNIP was obtained was 7.0 ± 3.7 and 7.4 ± 3.7 during, respectively, the first week's session and the second week's (p = 0.54, Wilcoxon). A trial effect without a week's session effect was observed ($p < 0.0001$ and p = 0.62, respectively, 2-factor ANOVA; fig. 2). In order to assess the possible fatigue effects of repeated SNIP we measured the mean difference between the maximal SNIP value and the value obtained at the last trial, and observed that it was less than the mean value of the coefficient of variation of SNIP (9 ± 3.5% and 7 ± 3.5% during the first and the second session vs. 10 ± 3.4%; table 2).

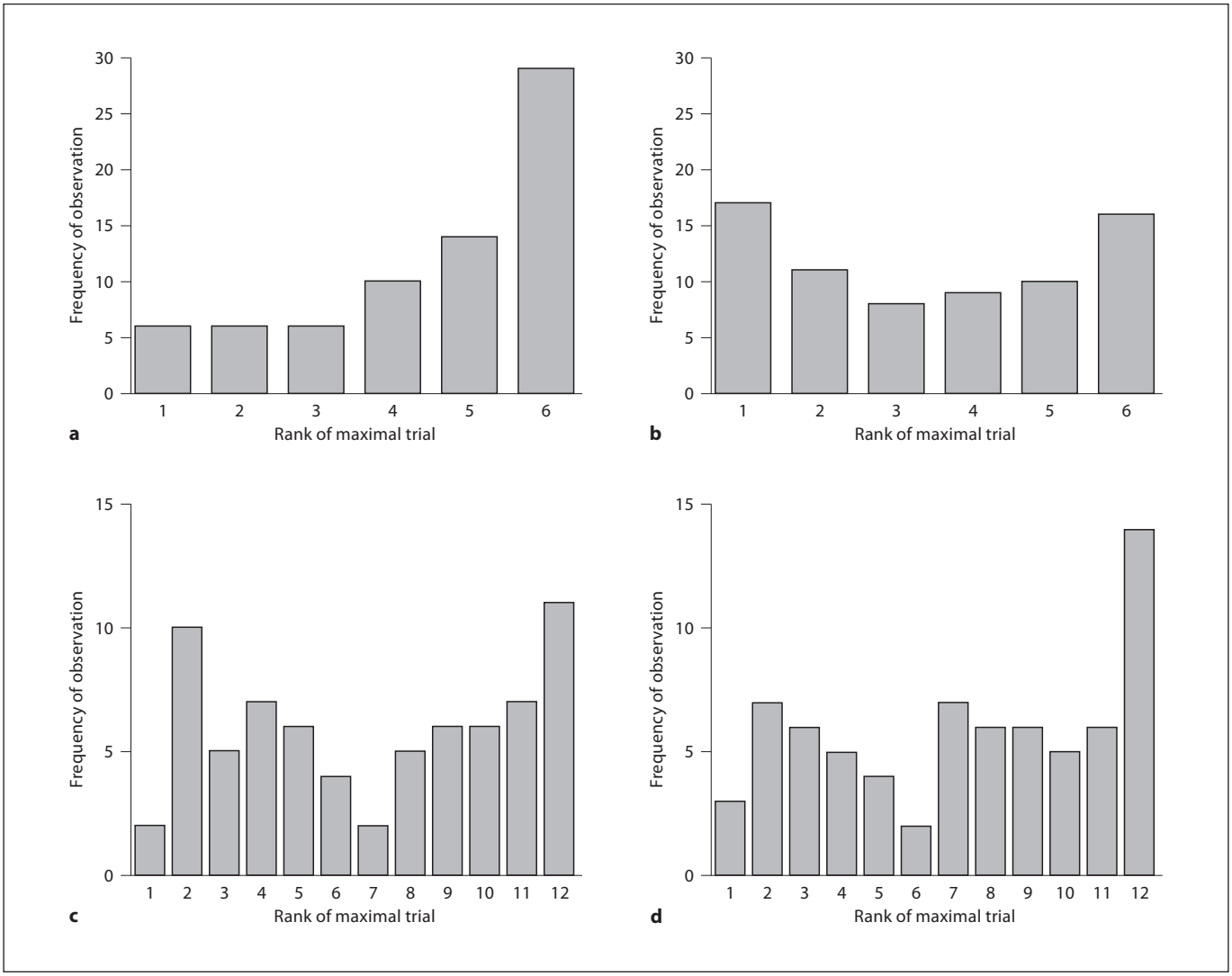

Fig. 1. Repartition of the rank of the maximal value for MIP and SNIP, for each week. **a** MIP during the first week. **b** MIP during the second week. **c** SNIP during the first week. **d** SNIP during the second week. All data are expressed as the frequency of observation.

Discussion

The present study observed that SNIP results were reproducible from session-to-session. In contrast, maximal MIP was higher and occurred earlier during the second session than the first. This suggests a learning effect with the MIP manoeuvre acquired during the first session, which remains and is maintained during the second session.

MIP is the most widely used volitional test for evaluating inspiratory muscle strength [6]. Although simple in principle, the MIP manoeuvre is difficult for many and requires a hermetic seal around the mouthpiece. Thus, several tests of inspiratory muscle function have been developed on the basis of the sniff manoeuvre, which is more natural to perform than the MIP. Reference values have been established for SNIP and MIP in adults and children [3, 6, 22, 28–30]. The within-session reproducibility of SNIP has been studied in adults and in children, giving conflicting results [7, 18, 31]. In a limited number of adults, with some of them being familiar with the technique, the reproducibility of SNIP appeared very good (and comparable to MIP), with a within-session coefficient of variation of 6% [18]. However, it was much poor-

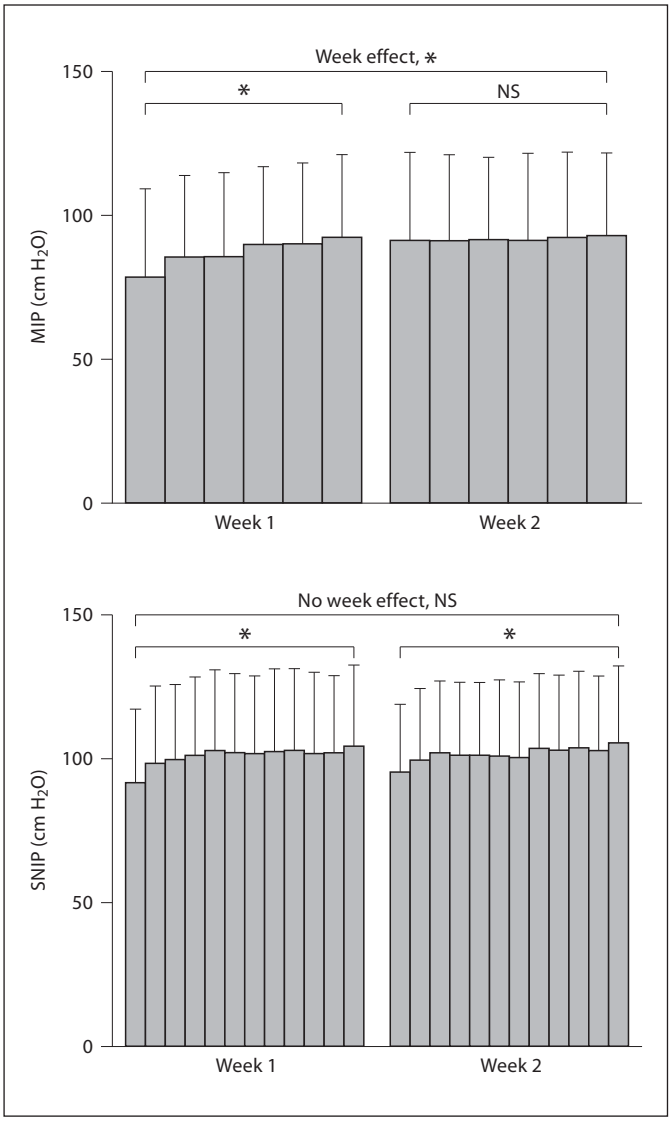

Fig. 2. Evolution of pressure measurement during the consecutive trials on each week. The week effect and the trial effect were evaluated in a 2-factor ANOVA for repeated measurements (trial effect and week effect). The trial effect was also analyzed independently each week using a 1-way ANOVA for repeated measurements. * $p < 0.05$; NS = not significant.

er in a larger number of unselected children, with a within-session coefficient of variation ranging from 16 to 26%, depending on the age group [7, 31]. Nevertheless, good reproducibility does not necessarily indicate maximal effort [27].

In contrast, poor within-session reproducibility could be neglected as a bad indicator of maximal value objective provided that the trial repetition is associated with a progressive increase in performance and a tendency to reach a plateau. This result indicates that either a learning effect or a warming-up effect is necessary to attain the maximal value. By exploring the session-to-session reproducibility, the differentiation between learning effect and warming-up effect could be addressed. If the performance increase is preserved and even improved from one session to the next, as we observed with MIP manoeuvres, it is certainly due to a learning effect. In contrast, if the performance increase is not conserved from one session to another, as we observed with SNIP manoeuvres, the hypothesis of a warming-up effect is more probable than a learning effect. A learning effect with the MIP manoeuvre across sessions has already been demonstrated in chronic obstructive pulmonary disease [32], in multiple sclerosis, [24] and in healthy subjects [33]. In addition, a warming-up effect independent of the learning effect was also observed with the MIP manoeuvre in healthy subjects [33]. Our results are in accordance with these previous studies. Indeed, we observed a week effect on maximal MIP, on the number of trials necessary to obtain maximal MIP, and when the repeated manoeuvres were compared between the 2 weeks. In contrast, no week effect was observed with the SNIP manoeuvre. This result strengthens the hypothesis that sniffing is a natural, spontaneous manoeuvre which does not need to be taught [29]. These data also suggest that the MIP manoeuvre is less reproducible than the SNIP manoeuvre. However, one can assume that once the MIP manoeuvre is learned, it could be as reproducible as the SNIP manoeuvre. But this learning period with the MIP manoeuvre is not easily applicable in clinical practice.

Our study was conducted on a group of selected young healthy medical students, aware of respiratory physiology, with normal lung function. We could expect that in this population the effect of learning is small and this would be conducive to doing a study on the effect of training on MIP and SNIP. Here, we demonstrate that the reproducibility for SNIP is higher than for MIP and that a learning effect is present for MIP, indicating that even in this selected population, learning remains a confounding measurement factor. We can expect that in the general healthy population, the learning factor increases the difference in reproducibility between SNIP and MIP.

Moreover, the study was performed on healthy subjects without nasal obstruction or pulmonary obstructive disease. However, as previously demonstrated, SNIP may underestimate inspiratory muscle strength in specific populations, such as individuals with nasal obstruction and patients with chronic obstructive pulmonary disease

[11, 34]. Therefore the fact that SNIP is preferable to MIP in short-term evaluation of respiratory muscle strength because of better reproducibility and a lower learning effect must be counterbalanced by the fact that in clinical situations, even without nasal obstruction or airway disease, the combination of the 2 test results increases the diagnostic precision compared to 1 test alone.

In this study, the time separation between the 2 sessions was set to 1 week. It was chosen in order to find a compromise between acute/sub-acute neuromuscular diseases such as Guillain-Barré syndrome or myasthenia gravis, and the chronic neuromuscular diseases. Previous studies were interested in reproducibility with 1 break of 1 day or 1 month. We cannot exclude the probability that a longer delay between sessions could decrease this difference, and this remains to be evaluated by further studies.

Underestimation of MIP would not be harmful for the patient, if it led to reinforcement of pulmonary rehabilitation. On the other hand, a false assessment of the evolution of MIP, for instance measuring a stable or slightly increasing MIP over time because of learning effect might overestimate the efficacy of new available treatments with promising results. For example, enzyme therapy with recombinant human acid α-glucosidase for the treatment of Pompe's disease, could be harmful [35, 36].

In conclusion, Steier et al. [3], have recently suggested performing multiple tests of respiratory muscle function in order to increase diagnostic precision. However, in the follow-up of inspiratory muscle performance we must take into account the fact that SNIP is less sensitive to learning effect than the MIP manoeuvre. It requires only a routine warm-up. In contrast, the maximal day value is obtained earlier with MIP manoeuvres, but this maximal value increases with repeated sessions, suggesting a session-to-session learning effect. This may reduce the interest of using MIP measurement for following patients. These results suggest that the SNIP manoeuvre is preferable to the MIP manoeuvre for monitoring inspiratory muscle performance evolution. These findings need to be confirmed by further clinical studies which include a group of patients with chronic neuromuscular disease.

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