Reports of Original Investigations

Automated respiratory inductive plethysmography to evaluate breathing in infants at risk for postoperative apnea

[La pléthysmographie inductive respiratoire automatisée pour évaluer la respiration chez les nourrissons présentant un risque d'apnée postopératoire]

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Purpose: Although respiratory inductive plethysmography (RIP) is the method of choice for the assessment of sleep disordered breathing, it has not been applied to the study of infants at risk for postoperative apnea (POA). The purpose of this study was to apply RIP to evaluate breathing in these infants. An additional purpose was to implement, simultaneously, three novel algorithms to detect movement artifact, respiratory pauses, and thoracoabdominal asynchrony, since their combined output both detects respiratory pauses and classifies them as obstructive or central in origin.

Methods: A prospective study design was employed to record the analogue output of RIP, saturation, and finger plethysmography in a convenience sample of infants. The data record underwent a dual analysis: 1) automated detection of respiratory events; and 2) visual coding of the cardiorespiratory data. A novel index, coined pause density, was calculated as the sum of all respiratory pauses.

Results: Twenty infants, whose mean postconceptional ages and weights were 44.47 ± 2.88 weeks and 4.21 ± 0.99 kg, respectively, were recruited. Data recording ranged from four to 24 hr. Ten infants (term = 5) experienced POA: central apnea = 5, mixed obstructive apnea = 6, and two former premature infants experienced both. Twenty-five central apneic events were detected, and the majority followed a sigh. Infants who experienced apnea also had high values of pause density.

Conclusion: Respiratory inductive plethysmography may pro-

vide a useful method to evaluate breathing in infants at risk for POA. The study of short respiratory pauses may prove useful in predicting apnea risk.

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Objectif : Bien que la pléthysmographie inductive respiratoire (RIP) soit la méthode privilégiée pour évaluer les troubles respiratoires du sommeil, cette technique n'a pas été employée dans l'étude des nourrissons présentant un risque d'apnée postopératoire. L'objectif de cette étude était d'utiliser la RIP pour évaluer la respiration de ces nourrissons. Un objectif secondaire était de mettre en œuvre trois nouveaux algorithmes pour détecter simultanément les artefacts de mouvement, les pauses respiratoires et l'asynchronie thoraco-abdominale, étant donné que la combinaison de ces données détecte les pauses respiratoires et les classe selon que leur origine soit obstructive ou centrale.

Méthode : Un devis prospectif a été utilisé pour enregistrer la sortie analogique de la RIP, la saturation, et la pléthysmographie digitale dans un échantillon de commodité de nourrissons. Le fichier de données a subi une analyse double : 1) détection automatique des événements respiratoires ; et 2) codage visuel des données cardiorespiratoires. Un nouvel indicateur, appelé densité des pauses, qui est égal à la somme de toutes les pauses respiratoires, a été calculé.

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Résultats : Vingt nourrissons, dont l'âge post-conceptionnel et le poids moyen étaient respectivement de $44,47 \pm 2,88$ semaines et $4,21 \pm 0,99$ kg, ont été recrutés. L'enregistrement des données allait d'une durée de quatre à 24 h. Dix nourrissons (5 à terme) ont présenté une apnée postopératoire : apnée centrale = 5, apnée mixte obstructive = 6, et deux nourrissons nés prématurément ont présenté ces deux types d'apnée. Au total, 25 événements apnéiques centraux ont été détectés, et la majorité sont survenus à la suite d'un soupir. Chez les nourrissons ayant manifesté de l'apnée, nous avons également observé des valeurs élevées de densité des pauses.

Conclusion : La pléthysmographie inductive respiratoire pourrait constituer une méthode utile pour évaluer la respiration des nourrissons présentant un risque d'apnée postopératoire. L'étude des courtes pauses respiratoires pourrait s'avérer utile pour prédire le risque d'apnée.

POSTOPERATIVE apnea (POA) is a clinical entity important to the practice of pediatric anesthesiology. Its incidence varies with the method used to detect apnea, the mode of data recording, the duration of expiration used to define apnea, the patient population, and the anesthetic practice.¹⁻⁶ In 1982, David Steward⁷ first reported apnea in 9% of infants during recovery from anesthesia. A study of infants undergoing pyloromyotomy reported that POA occurred in 16% of at-risk patients.² Gestational age and postconceptional age (PCA) predict the risk of POA, such that the risk for formerly premature infants is not less than 5% at a PCA of 48 weeks, and not less than 1% at a PCA of 56 weeks.¹ Both central and mixed obstructive apnea are reported: 71% and 21%, respectively.³ Apneic events occur in both the early and late postoperative course.^{1,3,4,8,9} At present, no physiologic index of breathing has been reported to predict the risk for apnea in infants following anesthesia, although two clinical reports suggest that the periodic breathing and multiple brief apneas in infants are breathing patterns at risk for POA.^{9,10}

Respiratory inductive plethysmography (RIP) has been used extensively to assess infants and children with sleep disordered breathing.¹¹⁻¹³ This research method has not been applied to the study of POA, which has primarily been studied with transthoracic impedance, nasal thermistry, and pneumograms.^{2-4,8,9}

We hypothesized that RIP was well suited to evaluate the breathing pattern in infants recovering from anesthesia. Since the data analysis would be greatly facilitated by a method that automatically detects respiratory pauses, we have developed algorithms

which measure the energy contained in the ribcage and abdomen signals of RIP and apply thresholds to detect both movement and pauses.^{A,B} In addition, we have developed an algorithm to measure the phase relationship between ribcage and abdomen, and we apply a threshold to define asynchronous breathing.¹⁴ The simultaneous implementation of these three algorithms to detect respiratory pauses and to classify the respiratory pauses as either central or obstructive in origin became possible in 2006. We present our results from a convenience sample of 20 infants at risk for POA.

Methods

The study was approved by the Institutional Review Board of McGill University Health Centre/Montreal Children's Hospital (Montreal, Quebec, Canada), and informed written parental consent was obtained. We conducted a prospective study in a convenience sample of 20 infants scheduled for elective herniorrhaphy. Potential recruits were identified to us by the pediatric general surgeon, and patients were recruited during preoperative anesthetic consultation. The surgeon and family determined the timing of surgery by weighing the relative risks of surgery and the potential for bowel obstruction. The inclusion criterion was PCA less than 60 weeks at the time of surgery. Exclusion criteria were emergency surgery, cardiorespiratory and neurological disease, and any contraindication to general anesthesia.

Segments from the data recordings of some of the infants have previously been published during the development of the novel analysis algorithms.^{A,B,14,15}

The anesthetic technique was standardized and included intravenous induction with atropine ($20 \mu\text{g}\cdot\text{kg}^{-1}$ *iv*), sodium thiopental ($3 \text{ mg}\cdot\text{kg}^{-1}$ *iv*), and anesthesia maintenance with either sevoflurane or isoflurane in a mixture of nitrous oxide and oxygen. Atracurium ($0.5 \text{ mg}\cdot\text{kg}^{-1}$ *iv*) was administered to facilitate intubation of the trachea. At the conclusion of surgery, neuromuscular blockade was reversed with neostigmine ($50 \mu\text{g}\cdot\text{kg}^{-1}$ *iv*) and atropine ($20 \mu\text{g}\cdot\text{kg}^{-1}$ *iv*). Infants were extubated awake in the operating

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room. Analgesia was provided with bupivacaine 0.25% with 1:100,000 epinephrine (1 mL·kg⁻¹) administered by caudal or ilioinguinal field block and rectal acetaminophen. No opioids were administered in either the intraoperative or postoperative period.

Upon arrival in the postanesthesia care unit, the RIP bands (NIMS Resptrace Plus, Miami, FL, USA) were placed around each infant's ribcage and abdomen and secured in place. A Nellcor N200 oximeter probe (Nellcor, Pleasanton, CA, USA) was taped to an extremity. The analogue output of the resptrace bands was amplified and filtered using a cut off frequency of 12 Hz, digitized, sampled at 50 Hz, and recorded on computer (LABDAT, RHT Infodat, Montreal, QC, Canada) for off-line analysis. The duration of data recording complied with our practice guidelines for apnea monitoring in term and former preterm infants at risk for POA, 4–12 and 12–24 hr, respectively.

Data analysis

Two methods were used to analyze the data record. The automated analysis simultaneously implemented three algorithms whose combined output detected respiratory pauses and classified them as either central or obstructive in origin. The visually coded data analysis included scrolling through the data record to identify respiratory events and visually verifying that all events detected by the automated detection program were correct. In addition, a secondary analysis of respiratory events (ANADAT 5.2, RHT-Infodat, Montreal, QC, Canada, 1994) linked the respiratory event to changes in saturation and determined the duration of the event. Each of the two analysis methods produced an EXCEL spreadsheet that was subsequently merged into a single spreadsheet for each infant by manual edits linked to the time variable. The primary outcome variable was the presence of apnea.

Automated data analysis

Detailed descriptions of the detection algorithms have been published.^{A,B,14} Since we had previously determined that movement artifacts in RIP data were signals with high energy content predominately at low frequencies (0 to 0.4 Hz), we developed an algorithm to assess the frequency distribution of the energy in RIP signals. Segments with high energy and low frequency content were labelled as movement artifact.^{A,B} Segments with very low energy were identified and labelled as respiratory pauses. We extended prior work¹⁵ to develop an algorithm, termed the thoracoabdominal synchrony (TAS) index, to calculate the synchronization between the ribcage and abdominal signals.¹⁴ Asynchrony was defined as a TAS index > 54°.

The novel feature in the current study was simultaneous implementation of the three detectors in an interactive, automated program (MATLAB, Version 7.0, Mathworks Inc., Cambridge, MA, USA). Respiratory pauses were classified as central in origin if the ribcage and abdomen signals were synchronous (TAS index < 54°) in the data segments which bracketed the pause. A pause was classified as obstructive in origin if the ribcage and abdomen signals were asynchronous (TAS index > 54°) in the data segments bracketing the pause.

The output of the pause detector also yielded a duration for the respiratory pause. The summation of all respiratory pauses, verified by visual inspection, divided by the total time in quiet breathing gave a novel variable coined pause density, a quotient modified from Galinkin *et al.*²

Visual scoring and secondary data analysis

Although the detection algorithms have been validated against simulated signals, they have not yet been validated in a prospective study design against the gold standard for RIP analysis, namely visual scoring by experts. Therefore the segments of movement artifact and respiratory pauses detected by the automated analysis were visually inspected for verification that they had indeed been correctly detected and that the respiratory pause had been correctly classified. The data record of each child was segmented, and each epoch was visually scored for movement artifact, technically poor data, and analyzable data. Analyzable data segments were scored for the presence of respiratory events, i.e., pauses and sighs. Pauses were identified, visually, by a prolongation of expiratory time. Sighs were identified as an augmented respiratory breath. The respiratory pauses and sighs identified by visual inspection were crosschecked in time with those identified by the automated detection program.

The automated analysis is primarily a detection program. Therefore, a secondary data analysis of the respiratory events was required to determine the duration of the respiratory pause and to link the respiratory pause to changes in saturation. In addition, visual coding and secondary analysis were required to evaluate the inspiratory time of a sigh.

Secondary analysis of respiratory pauses

The duration of expiration defining central apnea was 15 sec. Central apneas were visually inspected and classified as following a tidal breath (PTA) or following a sigh (PSA) (Figures 1 and 2). Mixed obstructive apneas (MOA) were defined as a respiratory pause ≥ ten seconds plus asynchrony between the abdominal

FIGURE 1 Representative figure of a post-tidal apnea (PTA) illustrating a central apnea following a tidal breath. The apnea is central in origin, since average thoracoabdominal synchrony (TAS) index for pre- and post-PTA periods were 27.4 and 24.1°, respectively, and there is no evidence of respiratory effort during the 19 sec expiratory pause (see Methods). The oxygen saturation did not change.

and ribcage signals during the pause. Consistent with guidelines from the American Thoracic Society,¹¹ a second definition of a MOA was also employed, i.e., asynchrony between the abdominal and ribcage signals plus a respiratory pause < ten seconds if the pause was followed by a 4% fall in oxygen saturation (Figures 3 and 4).

Pauses in excess of ten seconds were analyzed using an interactive program (ANADAT 5.2, RHT-Infodat, Montreal, QC, Canada, 1994). Start inspiration and end expiration were identified by onset of the upswing which followed the nadir of the abdomen signal. Inspiratory time (Ti) was defined as the time interval between start inspiration and peak of the abdominal excursion. Expiratory time (Te) was defined as the time interval between the peak of the abdominal excursion and end expiration.

Analysis of spontaneous respiratory sighs

In order to distinguish spontaneous respiratory sighs from brief movement artifacts and arousals, only sighs preceded by segments of regular breathing data were analyzed (Figure 2). Sighs which were at least twice the control Ti (see below) were defined by Ti. The ratio of the sigh Te and the preceding control Te was calculated (sigh/control Te). The sigh frequency was expressed as the number of sighs per hour of quiet breathing. Segments of breathing preceding a respiratory sigh, that visually appeared to be regular in both amplitude and rate for a minimum duration of 20 sec, were designated

FIGURE 2 Representative figure of a post-sigh apnea (PSA) showing a central apnea following a sigh. The apnea is central in origin, since the average thoracoabdominal synchrony (TAS) index for pre- and post-PSA periods were 15.7 and 21.6°, respectively, and there is no evidence of respiratory effort during the 17 sec expiratory pause (see Methods). The Δ oxygen saturation following the PSA was +2%.

FIGURE 3 Representative figure of a mixed obstructive apnea (MOA) not associated with desaturation. The total duration of the obstructive event, containing two pauses, was 13 sec. The pause is obstructive in origin, since the average thoracoabdominal synchrony (TAS) index for pre- and post-MOA periods were 85.4 and 134.1°, respectively (see Methods).

control data, and the abdomen signal was analyzed for the Ti and Te (ABREATH, ANADAT, RHT Infodat, Montreal, QC, Canada). This interactive software program identifies breath peaks and partitions breaths into inspiratory and expiratory segments. The inspiratory and expiratory times for each data segment were averaged to give a control inspiratory (control Ti) and expiratory time (control Te).

TABLE Demographic data, ordered by ascending

Patient	GA (weeks)	PCA (weeks)	Weight (kg)	Gender	Nerve block	File length (hr)	Good data (min)	Apnea type
1	32	39	4.3	M	Caudal	19.5	1,013	Both
2	30	39	3.5	F	Caudal	21.5	969	CA
3	28	41	3.6	M	Caudal	19.4	925	Both
4	29	42	2.5	M	Caudal	19.7	992	CA
5	34	42	3.9	M	Caudal	14.8	680	MOA
6	40	44	4.3	M	Caudal	3.3	135	MOA
7	38	44	4.9	M	Ilioinguinal	3.8	191	nil
8	39	44	3.8	M	Caudal	5.1	216	nil
9	37	45	5.5	M	Ilioinguinal	4.3	218	CA
10	37	45	5.4	M	Caudal	5	239	CA
11	31	45	3.2	M	Caudal	7.92	339	nil
12	38	45	3.8	M	Ilioinguinal	5.2	247	nil
13	40	45	4.3	M	Caudal	3.9	201	nil
14	26	46	2.5	M	Caudal	12.7	610	nil
15	32	46	4.5	M	Caudal	10.37	450	nil
16	39	47	4.8	M	Caudal	7.48	369	nil
17	35	48	5.7	M	Caudal	10.6	428	nil
18	39	48	3.5	F	Ilioinguinal	11.9	490	nil
19	38	48	4.8	M	Ilioinguinal	6.32	282	nil
20	37	49	5.9	M	Caudal	3.2	163	MOA

Both = CA and MOA, CA = central apnea, GA = gestational age, Nerve block = type of nerve block performed for analgesia during surgery, MOA = mixed obstructive apnea, PCA = postconceptional age.

FIGURE 4 Representative figure of a mixed obstructive apnea (MOA) followed by desaturation. The total duration of the pause was ten seconds. A brief movement artifact is seen on the ribcage and abdomen signals following the MOA. The pause is obstructive in origin since the average thoracoabdominal synchrony (TAS) index for breathing segments pre- and post-MOA were 99.9 and 85.8%, respectively (see Methods). The pulsatility in the plethysmographic signal is present throughout. The Δ saturation was -8%. The minimum saturation was 92%.

Analysis of saturation

The plethysmograph signal was visually inspected to ascertain that the pulsatility was present throughout the respiratory event. The change in saturation value during and immediately following the apnea was recorded as the saturation nadir following the apnea (Figures 1–4).

Results

Twenty-three infants were recruited to the study between July 1997 and June 2000. Two infants were excluded for technical problems with data collection. One infant was excluded due to deviation from the anesthetic protocol. Twenty infants (term = 11) were analyzed, and results are reported for these infants. The mean postconceptional age and weight were 44.47 ± 2.88 weeks and 4.21 ± 0.99 kg, respectively. Caudal blockade was performed in 14 infants (term = 6) (Table). Typically, the infants were sufficiently recovered from anesthesia to receive clear fluids by bottle within the first hour of admission to the post-anesthesia care unit, following which the infants were settled to sleep.

Two hundred hours of data were recorded and analyzed. Seventy percent of the data comprised quiet breathing.

Of the 4,908 respiratory pauses identified by the automated pause detector, 48 met the definitions of apnea, i.e., PSA = 39.6%, PTA = 12.5%, MOA = 47.9%. Ten infants (term = 5) experienced POA (central apnea = 5, MOA = 6), and two former premature infants experienced both central apnea and MOA. Twenty-five central apneas were recorded in five infants (term = 2). Twenty-three MOA were experienced by six infants (term = 3).

Most of the central apnea and central respiratory pauses ≤ 15 sec occurred early in the postoperative course (Figures 5 and 6). Although three term infants

FIGURE 5 Graphic showing the time course of the appearance of apnea in the post-operative period. The majority of central apnea (PTA = 6, PTA = 19) appear in the initial five hours following admission to the postanesthesia care unit (PACU), whereas the majority of mixed obstructive apnea ($n = 23$) occur five hours after admission to PACU.

experienced single episodes of MOA early in the post-operative course, more typically, there was a delay of several hours before the appearance of the MOA.

Nineteen (76%) of the central apneas followed a sigh. In the 15 infants with central respiratory pauses of ten seconds < 15 sec duration ($n = 124$), the majority (90%) were also preceded by a sigh. The mean for the value for the ratio of sigh/control T_e was 4.42 ± 1.62 ($n = 872$). The mean sigh frequency was 6.8 ± 2.27 sighs per hour of quiet breathing.

In one data record (patient #2, Table) the signal/noise ratio for ribcage was poor and precluded application of automated analysis, and the pause density could not be calculated in the remaining 19 infants. Postoperative apnea was seen most frequently in young infants and in infants with a high pause density (Figure 7).

Discussion

The simultaneous implementation of the movement, pause, and asynchrony detection algorithms is a novel aspect of this study that facilitated the automated detection of respiratory pauses and classification of the pauses as either central or obstructive in origin. The pause density, a summation of the respiratory pauses, is thereby an assessment of the regularity of the breathing pattern, since a perfectly regular breathing pattern with no prolongations in T_e would result in a zero value for pause density. Infants with a high pause density were more likely to experience apnea. This observation is consistent with reports that periodic breathing and multiple brief apneas are postoperative breathing patterns found in infants who experienced POA.^{9,10} In addition, a positive correlation between the occurrence of brief (3.6–6 sec) and long pauses

FIGURE 6 Cumulative graphic showing the appearance of respiratory pauses < 15 sec during the postoperative course for: post-tidal pauses (PTP = 3695), post-sigh pauses (PSP = 424), and mixed obstructive pauses (MOP = 741). The central pauses occurred earlier in the postoperative period than the mixed obstructive pauses. Fifty percent (arrows) of the total number of pauses for PTP, PSP, and MOP occurred at 3.8, 4.0, and 6.8 hr, respectively, following admission to the postanesthesia care unit.

FIGURE 7 Showing the relationship between post-conceptual age and the pause density for 19 infants. Closed circles denote infants who experienced apnea, whereas open circles denote infants who did not.

has been reported in sleeping, non-surgical infants.¹⁶ Periodic breathing and breathing patterns with multiple brief apneas would both result in a high value for pause density. Pause density has the potential to provide a physiologic index that might detect breathing patterns at risk for apnea as well as monitor recovery in infants at risk for POA.

Our choice of a 15 sec duration for expiration to define central apnea is consistent with a report pertaining to 110 term infants, aged 43 to 49 weeks PCA, in

which no pauses > 15 sec were recorded during 22 hr recordings of respiration.¹⁶ In addition, the Collaborative Home Infant Monitoring Evaluation (CHIME) group reported the occurrence of apnea, in excess of 20 sec, occurred in only 40% of infants, including the 306 term infants during an extensive recording period of one month.¹³ During our shorter recording period, 50% of infants experienced POA, supporting our notion that RIP could be a promising method to study apnea in the postoperative period.

The CHIME study reported that 50% of apneas, in excess of 20 sec, were associated with at least three obstructed breaths.¹³ During recovery from anesthesia, hypercarbia, reduced lung volumes, and the lingering effects of anesthetic agents would all tend to increase the collapsibility of the pharynx, predisposing infants to obstructive pauses and apnea.¹⁷⁻²⁰ However, Kurth *et al.*,³ recording in the initial two postoperative hours following anesthesia, reported that only 27% of apneas were of the mixed or obstructive type. We report that the majority of obstructive events occurred late in the postoperative course. This late appearance of obstructive apnea, in the context of POA, suggests that other factors were involved, possibly rapid eye movement sleep, a sleep stage known to be associated with obstructive apnea.^{21,22}

The co-localization of apnea and sighs in infants has long been recognized. During non-rapid eye movement sleep, the percent of apneas which followed a sigh in infants aged 39, 45 weeks PCA, and three months was 18%, 29%,²³ and 40%,²⁴ respectively. We report that the majority of central apnea and long pauses followed a sigh. This high prevalence of PSA and their appearance early in the postoperative period supports the notion of a transient exaggerated response to lung inflation, facilitating apnea during recovery from anesthesia. Both chemical and reflex mechanisms may be involved. A sigh abruptly increases oxygen tension and decreases carbon dioxide tension. An impairment in chemoresponsiveness, as has been reported following general anesthesia,²⁵ may have promoted the apnea following spontaneous sighs observed in our infants.

Although the dominant factor to which the respiratory system responds following a sigh is thought to be chemical,^{26,27} brief end-inspiratory airway occlusions, which apply a volume stretch to the pulmonary stretch receptors, can also prolong Te.²⁸ During tidal volume breathing, an end-inspiratory airway occlusion, which results in a prolongation of expiration by 25%, is indicative of an active Herring Breuer inflation reflex.²⁹⁻³¹ A twofold increase in the volume stimulus, as occurs following a spontaneous sigh, prolongs the Te tenfold.^{28,29} Even during spontaneous sighs, there

is a strong correlation between lung volume and peak pulmonary stretch receptor discharge frequency.³² Since general anesthesia may alter the central integration of (volume related) stretch receptor activity,³³ a volume related reflex mechanism promoting apnea following a sigh during recovery from anesthesia cannot be discounted in these young infants.

Respiratory inductive plethysmography has proven to be a robust and non-invasive method for the study of sleep disordered breathing. We submit that RIP is also well suited to the study of breathing in infants at risk for POA. Our initial experience with our automated analysis enabled us to detect respiratory pauses and to classify apnea type from RIP recordings. Our novel detection algorithms offer several advantages.^{A,B,14} They are applicable to a large class of sinusoidal and non-sinusoidal signals. They do not rely on a calibrated RIP system. The calibration routines which assign proportionality constants to the ribcage and abdomen signals, thereby allowing their summation to give a tidal volume,^{13,34-36} assume a fixed spinal angle, an assumption that is problematic with mobile infants, postanesthesia. The algorithms do not require segmentation of the data record into individual breaths. The asynchrony detection algorithm quantifies the phase relationship between the thoracic and abdominal signals, allowing an objective definition for asynchrony.

In conclusion, we report apnea in 50% of infants at age risk for POA. Novel findings were that the majority of central respiratory pauses and apnea occurred earlier in the postoperative course than was the case with mixed obstructive events. The majority of central apnea and long pauses followed a sigh, which may indicate a disturbance in central integration of both chemical and volume related input to respiratory control consequent to anesthesia. Our finding that infants who experienced apnea had a higher pause density suggests that broadening the study of POA to include an assessment of brief respiratory pauses may provide a physiologic index to predict both apnea risk and recovery from this risk in the postoperative period.

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