Auto-resuscitation by gasping and arousal and resuscitation effects of gasp, sniff- or hiccough-like aspiration reflex

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Abstract
- Gasping develops spontaneously during severe asphyxia and cardio-respiratory failure both in humans and animals to save their lives.
- This “auto-resuscitation by gasping” fails in very severe cases resulting in sudden death, e.g., Sudden Infant Death Syndrome (SIDS) or Sudden Cardiac Death (SCD).
- Nasopharyngeal stimulation in cats can regularly induce very similar reflex spasmodic inspiratory efforts, the so-called “aspiration reflex” (AR), which proved to be a very useful model for study of the development, therapy and prevention of acute cardio-respiratory failure.
- Several tested and hypothetic clinico-physiological implications indicate the useful function of AR in various stages of cardio-respiratory failure, including cardio-pulmonary-cerebral resuscitation (CPCR).

Methods
- Airflow (V) was recorded during intermittent induction of ~30% AR-30 min (6 cats) and quiet breathing (6 sham-operated controls) in sodium pentobarbitone anaesthesia (40 mg/kg i.p.).
- After human killing and complex histochemical preparation of the brainstem, c-Fos-like immunoreactive (FLI) dots indicating neuronal activation, were counted by a computer in 35 brainstem nuclei using stereotaxic atlas.
- Whole-night polysomnographic examination with >30 parameters was performed in 100 adults with sleep disordered breathing (SDB) divided into 5 groups of severity according to their apnoea-hypopnoea index (AHI).
- AH ÷5/h for snoring, AH < 5-10/h for upper airway resistance syndrome (UARS), AH >10-20/h, 21-40/h and >40/h for obstructive sleep apnoea syndrome (OSAS I, II and III), and development of gasping for asphyxia, were tentatively explained as a function of various forms of arousal and auto-resuscitation by gasping.

Results
- Significant 1,6-12 fold increase in the number of neurons activated by AR was observed in 14 of 35 brainstem nuclei, defined according to Bergman’s stereotaxic atlas.
- FLI dots were decreased in the medulla: commissural nucleus of NTS and FTL (11x), dorsal intermediate nucleus of NTS (9x), RBN, NA and NPA (5x), RFN, NA and NPA (12x). In the pons: COE, BC (11x), NPBL and KB (3x). In mesencephalon: FTC (1,6x).

Discussion
- Typical signs and symptoms in various types of arousal (Fig. 4):
  1. Sigh (augmented breath) and micro-arousal (<3 sec) for snoring.
  2. Hyperventilation, autonomic arousal and hyperventilation in UARS.
  3. Apnoic episodes with occasional chokes and arousal (<3-15 sec) in OSAS. Gradual prolongation of apnoea during the night reflects adaptation to lower O₂ saturations and represents preconditioning in asphyxia.
  4. Auto-resuscitation by gasping appears spontaneously in very severe asphyxia with gradual normalisation of blood pressure and gases, EEG activity and evoked potentials, as well as reappearing of spontaneous breathing in successful cases.
  5. Auto-resuscitation by gasping often fails during extreme asphyxia, particularly when combined with cardio-respiratory and thermoregulatory disorders, e.g. in SIDS and SCD.

References

Fig. 1: Reaction of normal and SIDS babies to asphyxia
- A healthy infant lying in prone position exposed to a lack of O₂ and CO₂ respiration with a startle reaction and a gasp with arousal to survive.
- A baby in a critical phase of development for insufficient cardiorespiratory and thermo-regulatory mechanisms (during 8 months from birth) does not react to the same stress by effective auto-resuscitation by gasping and silent death results.

Fig. 2: C-Fos detection of activation of brainstem respiratory, cardiovascular and RF neurons by AR
- Significant 1,6-12 fold increase in the number of neurons activated by AR was observed in 14 of 35 brainstem nuclei, defined according to Bergman’s stereotaxic atlas.
- FLI dots were decreased in the medulla: commissural nucleus of NTS and FTL (11x), dorsal intermediate nucleus of NTS (9x), RBN, NA and NPA (5x), RFN, NA and NPA (12x). In the pons: COE, BC (11x), NPBL and KB (3x). In mesencephalon: FTC (1,6x).

Fig. 3: Respiratory Arousal vs. Non-Respiratory Arousal in SDB
- Arousal from sleep increased in all patients, but resp. A increased and non- A decreased with the severity of SDB.
- In SAS III resp. A 79,8±15,3% was caused by severe hypoxemia AvgSatO₂ 86,6±12,2% (MxSEM) and MinSatO₂ 59,7±6,0%, p<0,05 for all, compared to other groups.

Fig. 4: Clinico-physiological implications of arousal, auto-resuscitation by gasping and CPCR by AR
- Normalisation of BP, Perfusion, neurological deficits, EEG, ECG.
- Interruption of hypoxic apnoea by gasp Normalisation of breathing.
- SIDS, Sudden Cardiac Death.
- Sinobronchial syndrome.
- Aspiration pneumonia.
- Termination of TIA, collapses comatose states (coma vigil?)
- Interruption of laryngobronchoscopy.

Conclusions
1. Arousal contributes to normalisation of disturbed vital functions (blood pressure, tissue perfusion, EEG, evoked potentials, ECG and breathing), but frequent interruption of sleep may result in daytime sleepiness, micro-sleep and accidents.
2. Spontaneous gasping can provide an effective auto-resuscitation from severe asphyxia, but its failure may result in SIDS or SCD.
3. The AR still persists during asphyxia and supports a development of aspiration pneumonia or sinobronchial synd.
4. AR is characterised by massive recruitment of brainstem respiratory, cardiovascular and RF neurons, detected by c-Fos study in cats. In addition to normalisation of disrupted vital functions, it can also interrupt functional disorders.
5. Results of systematic animal studies predisposes AR as a promising model for its wide application for animal experiments and Clinico-physiological studies.