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THE CYANIDE GASP AND SPONTANEOUS DEEP BREATHS

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Abstract. Stimulation of the carotid body chemoreceptors with cyanide in anaesthetized rabbits usually causes a deep breath or gasp, but only if the vagus nerves are intact. This gasp has several similarities with spontaneous deep breaths in eupnoea. In paralysed rabbits, artificially ventilated, chemoreceptor stimulation induces an augmented discharge in the phrenic nerve equivalent to a gasp. In spontaneously breathing rabbits spontaneous deep breaths are more frequent with hypoxia than with normoxia. The results are interpreted in relation to (i) positive feedback from the lungs and (ii) summation of chemoreceptor and tonic vagal drive causing augmented deep breaths.

Heymans, Bouckaert and Dautrebande (1931) reported that cyanide acting on arterial chemoreceptors caused animals to take one or more long deep breaths (gasps).

Using small doses of KCN (10–100 μg given either i.v. or into the common carotid artery) we have shown that cutting the vagi changes the character of this response of breathing (Fig. 1) in pentobarbitone anaesthetized rabbits.

Without vagal conduction the rabbits failed to gasp in response to cyanide. Moreover the time taken to reach peak ventilation was longer with the vagi cut than when they were intact and the animal gasped (Fig. 2). These were consistent findings in 10 rabbits.

The speed with which a rabbit reached its peak ventilation after a dose of cyanide depended upon it making a gasp and not simply on the integrity of its vagi. When a rabbit with vagi intact failed to gasp the time to peak ventilation was similar to that when the vagi were cut (Fig. 3 and 4).

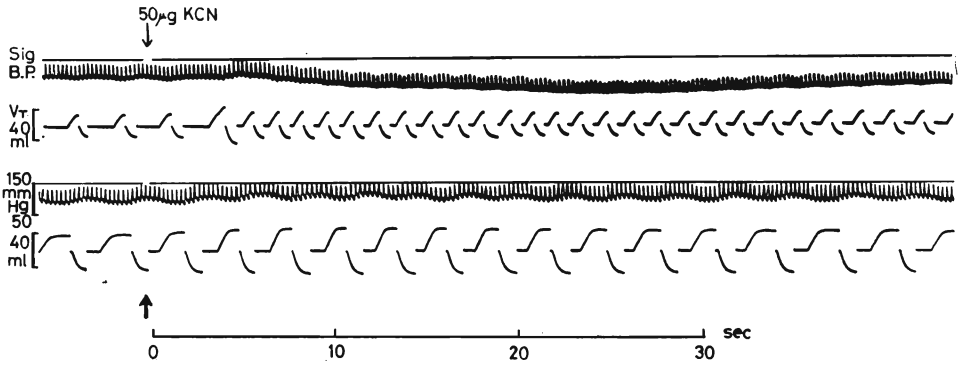

Fig. 1. Effect of 50 μg KCN injected into the right common carotid artery with vagi intact (upper record) and with vagi cut (lower record). Top trace, signal; middle, blood pressure; lowest, integrated pneumotachograph flow signal which zeros at points of no flow. Inspiration upwards.

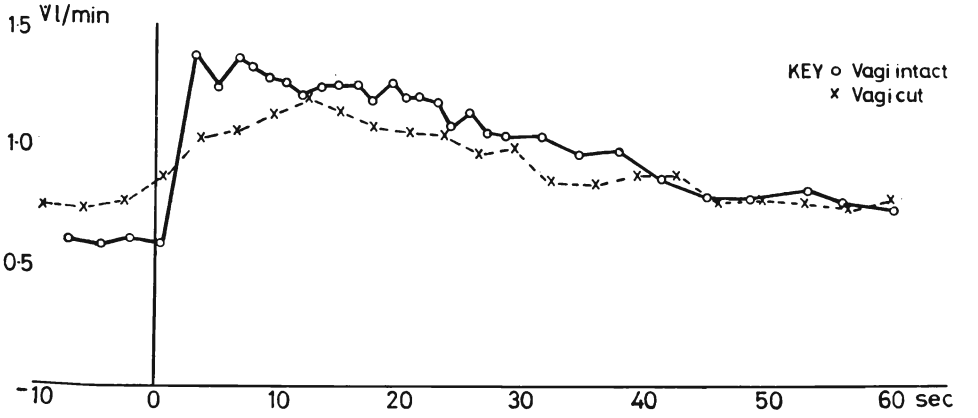

Fig. 2. The record in Fig. 1 plotted as breath by breath minute volume ($\dot{V}$) against time from KCN injection. Note that the peak ventilation is earlier before vagotomy.

Gasps provoked by cyanide have much in common with the spontaneous deep breaths which animals make occasionally during normal breathing (Larrabee and Knowlton 1964, Knowlton and Larrabee 1946, Reynolds 1962).

1. They are of the augmented breath pattern: inspiration starts as in a normal breath but then towards the time when the peak of a normal breath would come on augmentation of the inspiratory effort intervenes; one breath riding piggyback upon the other (Fig. 5).

2. Both spontaneous deep breaths (Knowlton and Larrabee 1946) and cyanide gasps require the vagi for their genesis.

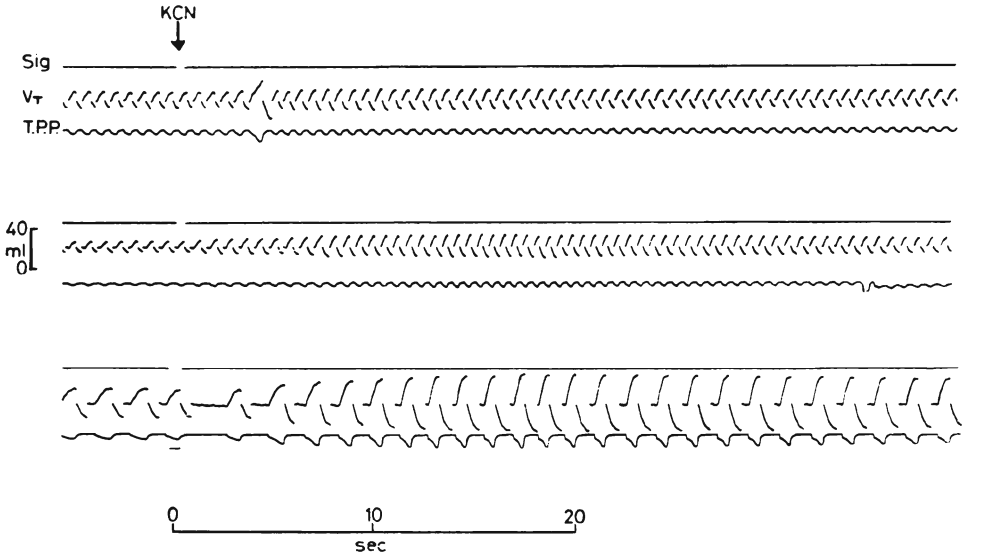

Fig. 3. Effect of KCN given into a common carotid artery. Upper record, 40μg before vagotomy resulting in a gasp; middle record, 30 μg before vagotomy, no gasp; lowest record, 40 μg after vagotomy, no gasp. Traces as for Fig. 1 with transpulmonary pressure replacing blood pressure.

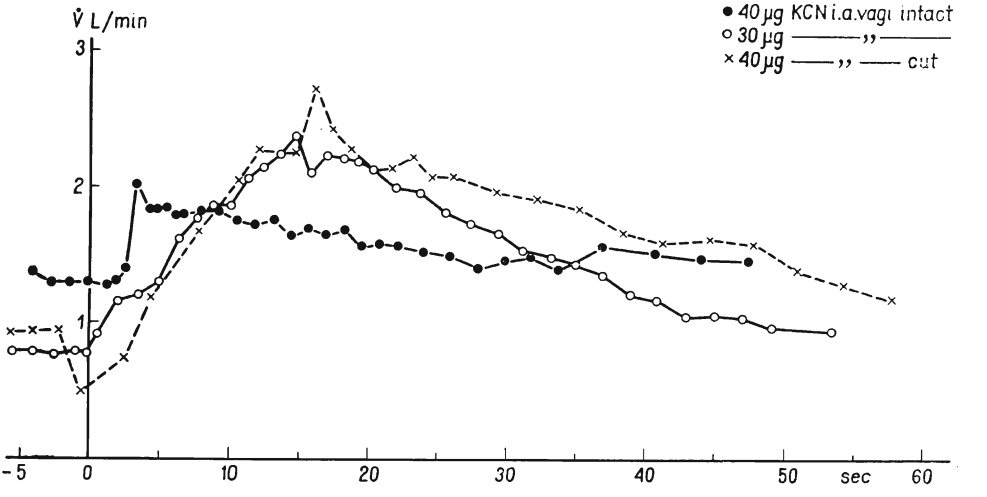

Fig. 4. Same data as in Fig. 3 plotted as breath by breath minute volume against time from injection of KCN.

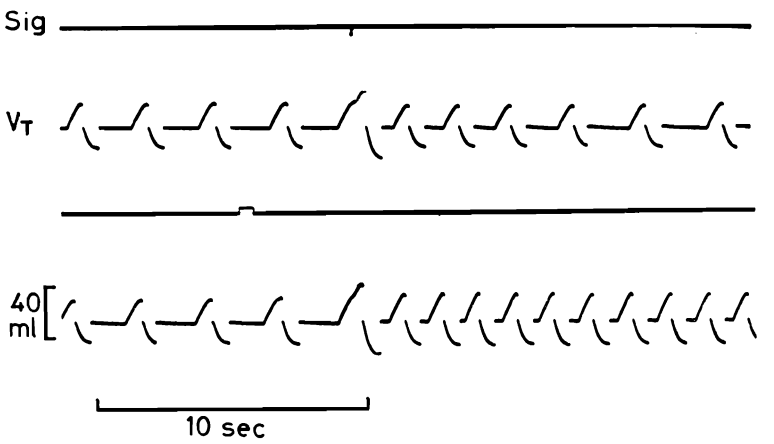

Fig. 5. Spontaneous and KCN sigh. Upper record: tidal volume trace showing a spontaneous augmented breath. Lower record: a KCN-induced augmented breath, after an injection of 50 μg KCN into the common carotid artery at signal.

3. The inspiratory phase of the deep breath itself is longer and deeper than preceeding (control) breaths whereas the succeeding breaths are more hurried than is usual for breaths of that depth (Reynolds and Hilgeson 1965, Euler et al. 1970).

4. Just as there is a "refractory period" after a spontaneous augmented breath during which it is difficult to elicit another deep breath by overinflation of the lungs (Reynolds 1962) so after a spontaneous deep breath the animals failed to gasp in response to cyanide. We have given 13 paired doses of KCN to three rabbits. One dose of the pair was given at a random time while the other dose was given immediately after a spontaneous deep breath. 12 out of the 13 random doses caused a gasp while only two of those following a deep breath succeeded. This difference is significant ($p < 0.01$). On this evidence we believe that the cyanide gasp is a special case of the spontaneous deep breath.

We have considered two explanations of their common mechanism. (i) By positive feedback from the lungs. Once cyanide starts to make the rabbit breath more deeply this might stretch the lungs sufficiently to elicit the vagal reflex augmentation of inspiration described by Knowlton and Larrabee (1946). (ii) Peripheral chemoreceptor drive might sum with vagal drive in the "respiratory centre" causing a gasp. To test the latter possibility we have recorded from a phrenic nerve root in two rabbits. After checking the animals' gasp response to 100 μg KCN, i.v. we paralysed and artificially ventilated them before repeating the dose. Even when paralysed, when tidal volume was steady, the animal gave a pattern of phrenic discharge characteristic of a gasp (Fig. 6).

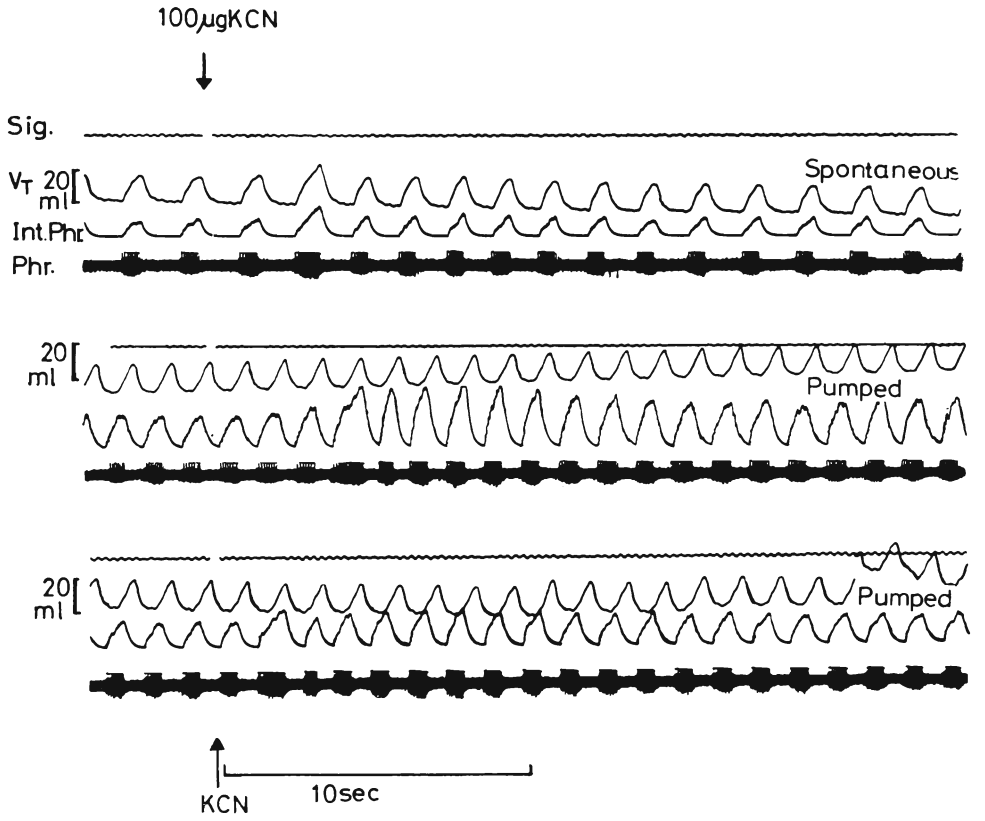

Fig. 6. Effect of a 100 μg KCN i.v. injection in a free breathing and subsequently paralysed rabbit. Volume trace as before except that there is no zeroing at times of zero airflow. The lowest traces are phrenic discharge (Phr.) and its integral (Int. Phr.). Integrated phrenic activity in the lower two records shows a gasp pattern despite paralysis.

This shows that peripheral chemoreceptor activity can sum with vagal activity to cause a gasp, but it does not rule out a lung reflex with "positive feedback" as an additional mechanism in rabbits which are allowed to increase tidal volume.

These results with cyanide suggested that chemoreceptor drive might play some part in the genesis of spontaneous deep breaths. To test this we switched the inspired gas mixture from air or 30% O_2 to 10% O_2 in four rabbits. This usually resulted in between one and three deep breaths over a period of 3 min (mean 1.5 sighs/change ofr 15 changes in gas composition). Switching from low to high O_2 seldom gave any deep breaths over the same period (mean 0.1 sigh/change for 15 changes in gas composition) (Table I). This difference is significant ($p < 0.01$).

TABLE I

Results of four experiments involving changes of inspired gas from high to low O_2 and low to high O_2. The numbers of sighs are totals for 3 min periods following each change of inspired gas $p < 0.01$

Rabbits	High to low O_2	Low to high O_2
R_m	4 changes 10 sighs	4 changes 2 sighs
R_n	2 changes 3 sighs	2 changes 0 sighs
R_o	6 changes 4 sighs	6 changes 0 sighs
R_p	3 changes 5 sighs	3 changes 0 sighs

Reininger and Segall (1970) with dogs and Bartlett (1971) with rats have recently published similar findings with hypoxia.

When the period of hypoxia extended beyond 5 min then the rate at which deep breaths occur tailed off. We are not yet certain whether chronically hypoxic rabbits take more deep breaths than normoxic ones.

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REFERENCES

BARTLETT, D. 1971. Origin and regulation of spontaneous deep breaths. Respir. Physiol. 12: 230–238.

EULER, C. von, HERRERO, F. and WEXLER, I. 1970. Control mechanisms determining rate and depth of respiratory movements. Respir. Physiol. 10: 93–108.

HEYMANS, D., BOUCKAERT, J. J. and DAUTREBANDE, L. 1931. Sensibilité des sinus carotidiens aux substances chimiques. Arch. Int. Pharmacodyn. 40: 54–67.

KNOWLTON, G. C. and LARRABEE, M. G. 1946. A unitary analysis of pulmonary volume receptors. Amer. J. Physiol. 147: 100–114.

LARRABEE, M. G. and KNOWLTON, G. C. 1946. Excitation and inhibition of phrenic motoneurones by inflation of the lungs. Amer. J. Physiol. 147: 90–99.

REININGER, E. J. and SEGALL, P. 1970. The effect of inhalation of O_2 and CO_2 gas mixtures on spontaneous gasps and apnea in unanesthetized dogs. Physiologist 13: 290.

REYNOLDS, L. B. 1962. Characteristics of an inspiration augmenting reflex in anesthetized cats. J. Appl. Physiol. 17: 683–688.

REYNOLDS, L. B. and HILGESON, M. D. 1965. Increase in breathing frequency following the reflex deep breath in anesthetized cats. J. Appl. Physiol. 20: 491–495.

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