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Time structure, temporal correlation and coherence of chemosensory impulses propagated through both carotid nerves in cats

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In spontaneously breathing, pentobarbitone anesthetized cats, we recorded simultaneously the impulses in the chemosensory fibers of both carotid (sinus) nerves, to analyze the correlations between the frequencies of chemosensory discharges (f_χ) and their activation ($\{df_\chi/dt\}_a$) and deactivation ($\{df_\chi/dt\}_d$) rates. We studied the chemosensory responses to brief exposures to hypoxia (100% N_2; 5-s and 10-s) and hyperoxia (100% O_2; 30-s), and intravenous injections of excitatory (NaCN 0.2-100 µg/kg) and inhibitory (dopamine hydrochloride 0.02-20 µg/kg) chemoreceptor agents. Hypoxia increased f_χ, with a high temporal correlation between frequency levels in both nerves. Prolonging hypoxic stimulation increased $\{df_\chi/dt\}_d$, with preservation of $\{df_\chi/dt\}_a$. Hyperoxic exposure produced highly correlated decreases in f_χ in both nerves, but reduced correlation in df_χ/dt. Increasing doses of NaCN produced analogous increments in f_χ, df_χ/dt and their correlations, the $\{df_\chi/dt\}_a$ / $\{df_\chi/dt\}_d$ ratio remaining constant along all the experimental range, except in one animal in which the ratio increased in both nerves alike. Dopamine reduced f_χ bilaterally, with chemosensory silencing being reached with doses of about 0.2-0.5 µg/kg, the correlations between f_χ's of both nerves remaining constant within the range analyzed. Maximal $\{df_\chi/dt\}_d$ was not affected along the range of dopamine doses, except in one animal in which it increased in both nerves. It is concluded that both carotid nerves convey similar quantitative information to the brain stem. Thus, the carotid nerves constitute either cooperative inputs or redundant afferences contributing to a high safety factor.

Key terms: *carotid (sinus) nerves; chemosensory activity; coherence; redundancy; time correlation*

INTRODUCTION

A central question in the study of an afferent pathway is how its impulse activity is determined by the intensive and temporal characteristics of the stimuli acting upon its receptive field, a problem which is commonly searched by testing the consistency ("reproducibility") of responses to repeated identical stimuli (*e.g.*, Wu *et al*, 1994). Essentially the same problem is posed by the coherence (Christakos, 1994) of impulse trains carried by homologous nerves in response to a single stimulus, but being a

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common receptive field rather exceptional, this is commonly studied by comparing the responses to two identical stimuli applied simultaneously to their respective receptive fields. But, this is difficult to achieve in practical terms.

The innervation of a common compartment by homologous nerves would constitute an ideal situation for the study of the problem referred to above. The carotid bodies "taste the blood", as cleverly assumed by de Castro (1928), and they convey their sensory information to the brain stem through the bilaterally located carotid (sinus) nerves. However, in humans and in the majority of mammalian species, the blood supply of the carotid bodies is provided by the carotid arteries, originated directly or indirectly from the aortic arch at different distances from the aortic valves of the heart (Adams, 1958), introducing different delays and the possibility of minor quantitative changes in the blood circulating through these sensing organs. Thus, the circulation time for drugs injected into a peripheral vein will be shorter for the right carotid body than for the left one in these animals. However, in the cat, both common carotid arteries are derived from the brachiocephalic (innominate) artery (Crouch, 1969), thus providing similar intensive and temporal characteristics for the blood circulating through the carotid bodies. Therefore, we took advantage of this anatomical condition to study the intensive and temporal features of the impulse trains recorded simultaneously from the chemosensory fibers of both carotid nerves in response to chemical stimuli introduced into the systemic circulation, in order to analyze their temporal correlations and coherence.

An important reason to address the above problem is that all studies correlating chemosensory inputs with ventilatory outputs require sectioning of one carotid nerve for the recording of its impulse activity and are thus based on the assumption that the chemosensory activity of the contralateral intact carotid nerve is strictly coherent with that recorded from the interrupted nerve. But that assumption merits experimental testing.

METHODS

Experiments were performed on 4 male adult cats, weighing 3.54 ± 0.38 kg (mean ± SEM), anesthetized with sodium pentobarbitone 40 mg/kg ip and receiving additional doses iv when necessary. The cats were placed in supine position. Body temperature was maintained at 38.0 ± 0.1°C with an electrically heated pad, placed beneath the cat, regulated by an automatic temperature controller receiving feedback from a thermistor probe introduced 5 cm into the rectum.

Cats breathed spontaneously throughout the experiments, via a tracheal cannula connected to a heated Fleisch pneumotachograph, allowing continuous recording of tracheal air flow and tidal volume. End tidal CO_2 pressure, continuously monitored through a fine sampling tracheal tubing and an infrared gas analyzer, was kept between 35 and 40 Torr. The left femoral artery was cannulated for arterial pressure recording, through a Statham pressure transducer, and the right saphenous vein was cannulated for drug administration. Physiological variables were continuously displayed on a polygraph.

The carotid bifurcations were exposed through a longitudinal midline neck incision and the sympathetic ganglio-glomerular nerves were cut at both sides. Carotid barodenervation was achieved by crush and section of nerve filaments between the carotid body and sinus (Zapata *et al*, 1969) at both sides. The carotid nerves were dissected bilaterally and cut at their apparent emergence from the glossopharyngeal nerves. After excision of epineurial sheaths, carotid nerves were placed on pairs of platinum electrodes and covered with mineral oil. The neural signals were preamplified, amplified, and filtered through bandpass (100 Hz to 1 Khz; -3 dB) and notch (50 Hz) filters prior to display on a multiple beam oscilloscope and storage on a digital video system for later analyses. The neural signals were digitized off-line using a 12-bit analog-to-digital (A/D) converter (Lab-Master DMA; 100 kHz) and commercial software (AxoTape, Axon Instruments, Inc). The signals were amplified to obtain maximal resolution in the A/D scale (± 5 V) and acquired at 5 kHz (see recordings displayed in Fig 1). The frequencies of chemosensory discharges (f_χ's) from both carotid nerves were derived from the digital records using a custom computer program that counted the number of spikes, over a given threshold, within 1-s successive periods. The f_χ's of both carotid nerves were stored on ASCII files. The rate of change of the frequency of chemosensory discharges on each second (df_χ/dt) was calculated, from the frequency files data, using Lagrange 3-point interpolation formula: $f'(x_1) = [f(x_2)-f(x_0)]/2h$, where $f'(x_1)$ is the derivative at point x_1, $f(x_2)$ is the value of the function at point x_{1+h} (x_2), $f(x_0)$ is that value at point x_{1-h} (x_0), **h** being the interval between consecutive points (1-s, in our case).

We analyzed the excitatory chemosensory responses to hypoxic hypoxia (produced by 5- and 10-s inhalations of 100% N_2) and to cytotoxic hypoxia (elicited by iv injections of NaCN 0.5 to 100 µg/kg), as well as the depressant chemosensory responses to hyperoxia (elicited by 100% O_2 inhalation for 30-s) and to iv injections of dopamine hydrochloride (0.01 to 20 µg/kg in saline, supplemented with 1 mM ascorbic acid to prevent oxidation). The secondary ventilatory responses to these stimuli were prevented by the bilateral carotid neurotomy. Temporal relationship between the chemosensory responses of both carotid nerves was assessed by linear correlation between f_χ's of both ca-

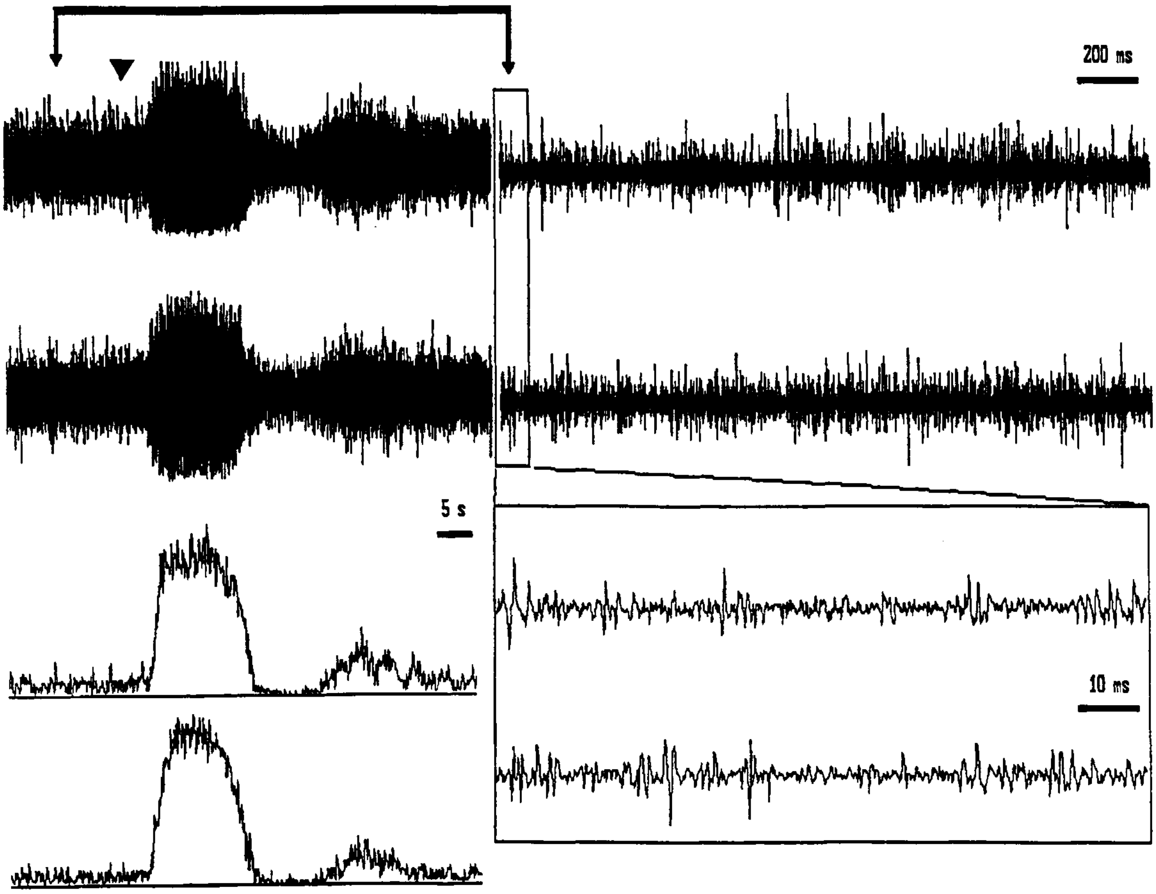

Fig 1. Recordings stored and redisplayed through system described in Methods. Left part, simultaneous recordings of chemosensory activity from both carotid nerves (upper quadrant) and instantaneous displays of their corresponding frequencies of discharges (lower quadrant), at slow speed; bursts of impulses evoked by iv injection of NaCN 100 µg/kg (at arrowhead). Right part, selected periods of basal chemosensory activities of both nerves simultaneously displayed at medium (upper quadrant) and fast (lower quadrant) speeds.

rotid nerves of each cat. Differences in responses to stimuli of different strengths and durations were assessed by Wilcoxon's matched pair tests. Differences were deemed as statistically significant when $P < 0.05$.

Experiments here reported were performed in accordance with the "Guiding Principles in the Care and Use of Laboratory Animals", endorsed by the American Physiological Society.

RESULTS

The electrical recordings obtained from both carotid nerves of the same cat presented different number of active fibers, depending on the damage caused by nerve dissection, the position of the nerve on the electrodes, and the distance between the electrodes. Three animals presented equivalent basal frequencies of chemosensory activities in both nerves, while one cat presented few active chemosensory fibers in one carotid nerve.

Chemosensory responses to hypoxic hypoxia.

Breathing 100% N_2 produced increases in f_χ in both carotid nerves, with very high correlations (r>0.96) between them in those animals with profuse chemosensory activity derived from multiple fibers (Fig 2A), but such correlation was lower (r=0.74) in the animal in which one of the nerves retained only few active fibers. The intensity and duration of the increases in f_χ above baseline were proportional to the duration of the hypoxic challenge, with a slight increase in correlation between f_χ's for those stimuli of longer duration (10-s *vs* 5-s) in three cats, while increasing stimulus duration reduced correlation in the cat presenting a low fiber count.

Two nerves that reach a similar maximal frequency of discharge in response to a given stimulus do not necessarily follow the same temporal profile in their increases in sensory discharges, as in their return to basal activities. Nevertheless, the activation ($\{df_\chi/dt\}_a$) and deactivation ($\{df_\chi/dt\}_d$) rates of the responses to hypoxic tests were similar between most pairs of nerves (Fig 2B) at both stimulus durations, with a high correlation between them (r>0.87). However, the cat with few active fibers nerve presented a lower correlation (r=0.56) at short stimulus duration (5-s), which was further reduced at longer stimulus duration (r=0.31).

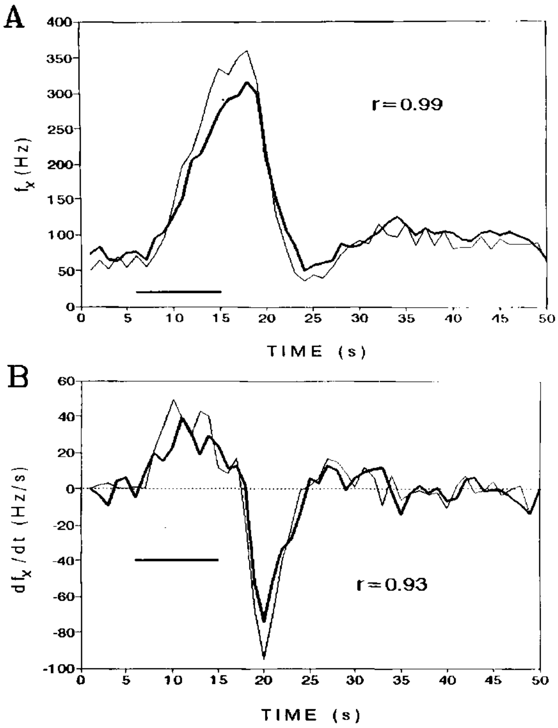

Fig 2. Changes in frequencies of chemosensory discharges (f_χ) (**A**) and in rates of change of those frequencies (df_χ/dt) (**B**) recorded from both carotid nerves (thin and thick lines) of one cat in response to hypoxic stimulation (breathing 100% N_2 for 10-s, horizontal lines). Insets, correlation coefficients. In B, activations (positive deflections) shortly after switching to 100% N_2 breathing, followed by deactivations (negative deflections) upon returning to air breathing.

A summary of activation and deactivation rates for hypoxic responses recorded simultaneously from both carotid nerves in four animals is illustrated in Figure 3. The procedure of plotting the carotid nerve reaching the higher $\{df_\chi/dt\}_a$ in response to 5-s N_2 tests in each cat in the x-axis results in the departure of the common slope from the identity line. The separate slopes for activation and deactivation rates adjust extremely well to the common slope for both types of rates. Furthermore, activation and deactivation rates were similar during 5-s

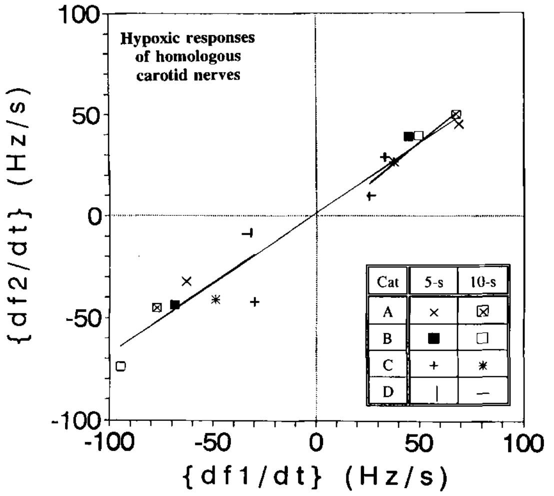

Fig 3. Summary of correlations in maximal activation (upper right quadrant) and deactivation (lower left quadrant) rates of chemosensory activities recorded simultaneously from both carotid nerves (x and y axes), along responses to breathing 100% N_2 for 5- and 10-s. Data from four cats. Inset, symbols for animals and stimuli durations.

stimulation, but prolonging the hypoxic stimuli to 10-s significantly increased the maximal deactivation rate ($p < 0.05$; Wilcoxon's signed rank test; not illustrated in the figure), without significantly modifying activation rates, as expected for stimuli varying in duration but not in strength.

Thus, hypoxic hypoxia produced chemosensory activation in both carotid nerves that followed a similar pattern, even when one nerve presented low activity.

Chemosensory responses to NaCN stimulation.

Increasing NaCN doses from 2 to 100 µg/kg produced bilateral, dose-related increases in f_χ, as illustrated in Figure 4A, the larger responses exhibited by one carotid nerve at all doses being presumably explained by the recording of a slightly larger number of sensory units from that nerve, which also would explain the apparently increasing divergence in total number of impulses recorded from both nerves as doses were increased. However, the increments in f_χ exhibited by both carotid nerves were highly correlated in all cats and the correlation raised with increasing NaCN doses (Fig 5A).

Similarly, both $\{df_\chi/dt\}_a$ and $\{df_\chi/dt\}_d$ increased in a dose-dependent manner (Fig 4B), and the correlation for rates of frequency change (df_χ/dt) of paired nerves also increased with larger NaCN doses (Fig 5B). The ratio between activation and deactivation rates remained constant along the whole range in most animals. In one animal, $\{df_\chi/dt\}_a$ increased in a steeper way than $\{df_\chi/dt\}_d$ when increasing NaCN doses, but this was observed for responses evoked from both nerves.

Since all injections were administered along 1-s periods, larger doses provided not only stronger stimuli (resulting in higher max f_χ) but also stimuli increasing at faster rates. This was shown by the shorter delays and shorter times to max f_χ's in responses to larger doses (Fig 4A), but also in more pronounced activation rates (Fig 4B).

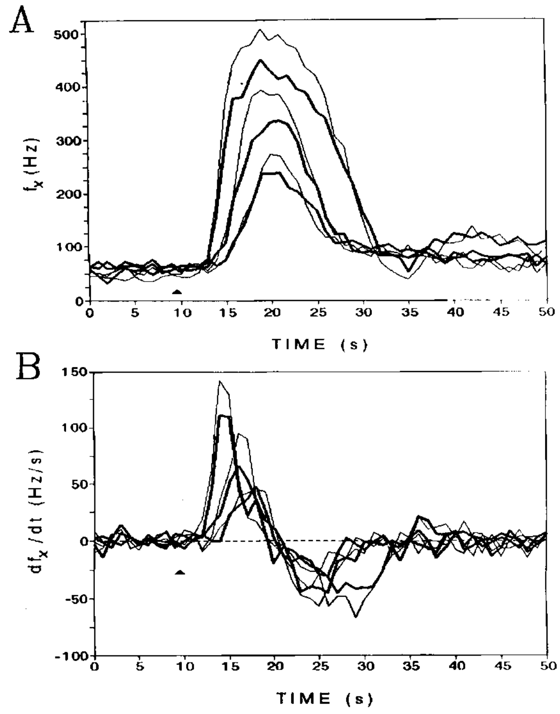

Fig 4. Chemosensory frequencies (A) and rates of change of such frequencies (B) recorded from both carotid nerves (thin and thick lines) in one cat in response to iv injections (arrowheads) of NaCN 2, 5 and 20 µg/kg (lower, mid and higher pairs of lines, respectively).

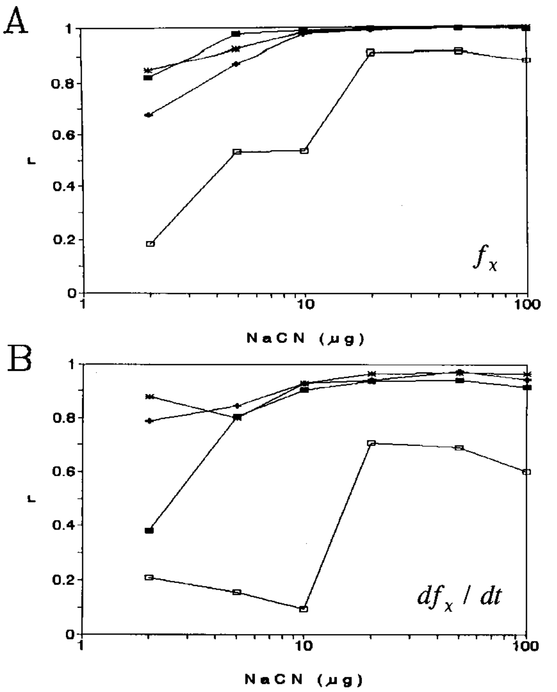

Fig 5. Correlation coefficients (r) between chemosensory frequencies (f_χ) (**A**) and rates of change of such frequencies (df_χ/dt) (**B**) recorded from both carotid nerves for the responses to increasing doses of NaCN given iv. Data from four cats (different symbols), the lower correlations corresponding to the animal with few-fibers recording in one carotid nerve (open squares).

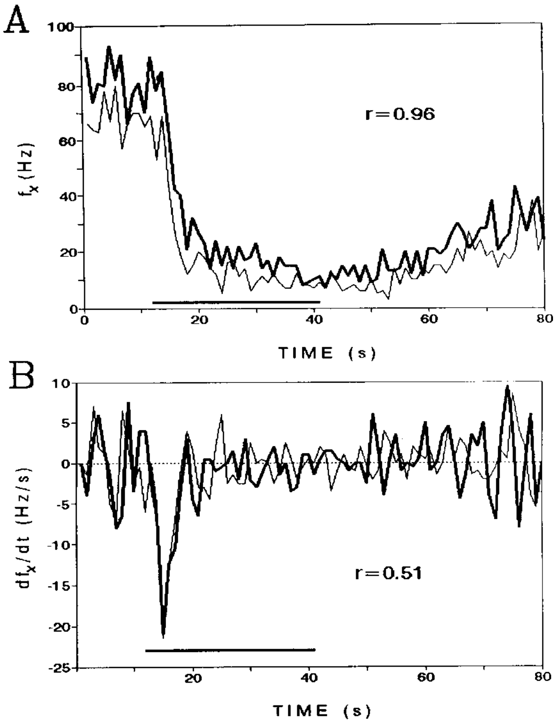

Fig 6. Changes in frequencies of chemosensory discharges (f_χ) (**A**) and in rates of change of those frequencies (df_χ/dt) (**B**) recorded from both carotid nerves (thin and thick lines) of the same cat in response to hyperoxic test (breathing 100% O_2 for 30-s; horizontal lines). Insets, correlation coefficients.

Chemosensory respons to hyperoxic tests.

Breathing 100% O_2 produced a profound reduction in f_χ in both nerves (Fig 6A). The correlation between the f_χ responses of both nerves to hyperoxia was high (r>0.9) in the three cats with high levels of basal f_χ because of multifiber recordings, but the correlation was lower (r<0.76) in the cat in which one carotid nerve had few active fibers and in which basal f_χ was low (not illustrated).

The analysis of df_χ/dt during the hyperoxia shows pronounced deactivation phases in both nerves shortly after the beginning of this test (Fig 6B). Moreover, when wide ventilatory fluctuations occurred during the basal normoxic condition (as in the cat whose recordings are illustrated in Fig 6), these concomitant oscillations were dampened during hyperoxia and recovered to their basal amplitude within about 30-s after the end of the maneuver.

Chemosensory responses to dopamine injections.

Dopamine injections induced marked reductions in f_χ, chemosensory activity becoming almost abolished shortly after doses larger than 0.2 to 0.5 μg/kg (Fig 7A). The larger doses of dopamine induced also a rebound in f_χ, closely associated with the ventilatory depression induced by these large doses. Since both carotid nerves had been interrupted in these experiments, this is probably originated from central ventilatory depression induced by concomitant hypertensive reactions (Zapata & Zuazo, 1980).

In response to dopamine injections, the rate of change of chemosensory discharges (df_χ/dt) presented a reduction (deactivation) followed by recovery towards basal activity (activation), deactivation being more intense but briefer than activation, as illustrated in Figure 7B. Here, the cyclic (respiratory) fluctuations, exhibited concomitantly by both nerves in basal conditions, were suppressed or attenuated by dopamine.

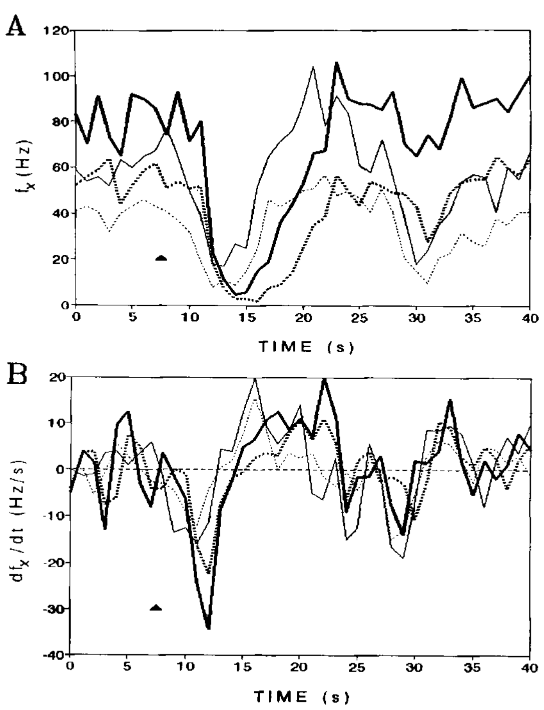

Fig 7. Changes in frequencies of chemosensory discharges (f_χ) (**A**) and in rates of change of those frequencies (df_χ/dt) (**B**) recorded from both carotid nerves (continuous and interrupted lines) of the same cat in response to iv injections (arrowheads) of dopamine hydrochloride 10 and 20 µg/kg (thin and thick lines, respectively).

DISCUSSION

A main problem in the study of neural systems is whether or not correlations exist between the unitary (single neurons or fibers) activities of a neuron population and how strong and widespread these correlations would be (Christakos, 1994). The temporal coherence of neural discharges carried along parallel channels (Perkel & Bullock, 1968) has been usually addressed by the simultaneous recording of nerve impulses along two "single units" of a nerve trunk or tract. However, here we are not concerned with the problem of unit-to-unit correlations within one carotid nerve, from which the homogeneity of chemosensory fiber responses within each nerve has been derived (Fitzgerald, 1976; Goodman, 1974), but we are interested in the aggregate-to-aggregate correlation of discharges carried by the two carotid nerves of a given animal, to find out if they convey essentially identical information.

Present results indicate that the chemosensory discharges of both carotid nerves of the same cat present a high degree of covariation in response to chemosensory stimulants and depressants. The ventilatory fluctuations in the instantaneous frequencies of basal chemosensory discharges recorded from both carotid nerves in some cats are also closely in phase (Alcayaga *et al*, 1996). If the carotid nerves were intact, this would result in synchronization of their chemosensory impulses impinging upon the solitary tract nuclei. Thus, ventilatory responses might be elicited by the "cooperative firing activities" (Gerstein *et al*, 1985) occurring simultaneously along these inputs.

After labeling with horseradish peroxidase, central projections of afferent fibers contained within carotid nerves (barosensory and chemosensory fibers) have been traced mostly to the ipsilateral lateral and medial nuclei of the solitary tract complex, whereas the commissural nucleus receives bilateral projections from both carotid nerves in cats (Berger, 1979; Ciriello *et al*, 1981; Nomura & Mizuno, 1982; Panneton & Loewy, 1980) and in rats (Seiders & Stuesse, 1984). However, convergence of carotid nerve chemosensory fibers may occur not only at the first relay station, but also at the following levels of brain stem structures involved in the generation of ventilatory output. It must be noted that, in contrast to most reflex pathways, ventilatory chemoreflexes are not lateralized (Berger & Mitchell, 1976; McQueen & Ungar, 1971).

What happens if the discharge frequencies of carotid afferents are dissociated? We observed that the unilateral intracarotid administration of dopamine –that transiently reduces or silences the discharges of one carotid nerve only– results in minimal or no depression of ventilation, while the same injection evokes consistent transient ventilatory depression when repeated after severance of the contralateral carotid nerve (Zapata & Zuazo, 1980). Thus, respiratory controlling bulbar structures appear to disregard falls in f_χ arriving through one carotid nerve if the contralateral homologous nerve continues carrying a normal rate of chemosensory discharges; but, in the absence of this comparative input, the same falls in f_χ are translated into transient depression of the chemosensory drive of ventilation.

If the chemosensory responses carried by both carotid nerves have similar time courses, will their input upon medullary structures result in simple addition of ventilatory reflexes? While studying the integrated phrenic nerve activity evoked by submaximal electrical stimulation of either one or both carotid nerves in chloralose-urethane anesthetized cats, Eldridge *et al* (1981) observed that the combined stimulation of both nerves did not show an algebraically additive effect, but the response was *ca.* 70% of that predicted from the summation of the responses to the stimuli when administered individually. Otherwise, Felder and Heesch (1987) found that nearly half of extracellularly recorded units from the solitary tract nucleus region of the dorsomedial medulla of the cat were excited by separate electrical stimulation of both carotid nerves and that summation of these inputs occurred upon simultaneous bilateral stimulation, but the barosensory and/or chemosensory nature of the electrically stimulated fibers was not determined.

Since the present observations show that both carotid nerves carry essentially similar chemosensory information, which will be the result of suppressing one of these afferences? In pentobarbitone anesthetized cats, the fast block of conduction by topical application of lidocaine to one carotid nerve causes a variable transient depression of ventilation, after which basal ventilation does not differ from control conditions (Eugenin *et al*, 1989). Nevertheless, analysis of the dose-response curves for the ventilatory effects induced in these cats by iv injections of NaCN revealed a minimal reduction in sensitivity after unilateral carotid neurotomy, compared to the pronounced decrease observed following bilateral carotid neurotomy. Otherwise, the reduction in tidal volume reactivity after unilateral carotid neurotomy approximately halved that induced by bilateral carotid neurotomy. Partly different results were observed in pentobarbitone anesthetized rats breathing gas mixtures which O_2 content varied between 21% and 8%, animals in which ventilation was not significantly decreased by unilateral carotid nerve section, while significant reductions in ventilation were observed after bilateral carotid neurotomy (Cragg & Khrisanapant, 1994). These observations indicate that a variable part of the information conveyed by both carotid nerves is treated as redundant input by the medullary structures involved in ventilatory regulation. Each carotid nerve also provides a variable contribution to the cardiovascular responses to hypoxia observed in spontaneously breathing, pentobarbitone- or chloralose-anesthetized cats (Serani *et al*, 1983), but it is rather difficult to assess the separate *vs* combined participation of the chemosensory afferents carried by both carotid nerves in cardiovascular regulation, because carotid neurotomies also interrupt the more important reflex role played by the carotid sinuses barosensory fibers conveyed by the same carotid nerves.

In view of the present results and above considerations on respiratory regulation, the cat carotid nerves may be considered as replicated afferent pathways, conveying redundant information on the composition of the blood. However, in two of the above mentioned studies on ventilatory reflexes (Cragg & Khrisanapant, 1994; Eugenin *et al*, 1989), the contributions of the two carotid nerves were of slightly different strengths. It must also be mentioned that in cats subjected to chronic unilateral petrosal ganglionectomy (producing degeneration of both peripheral and central processes of carotid chemosensory neurons), an enhancement of the contribution of the contralateral carotid nerve to ventilatory reactions induced by iv injections of NaCN was observed (Eugenin *et al*, 1990). Since present results indicate that afferent discharges recorded simultaneously in both carotid nerves in response to chemical stimuli show quite coherent patterns, the apparent lateralization of inputs (or their modification) with regard to eliciting ventilatory reflexes would depend on different degrees of divergence (spatial multiplication factor) or synaptic gains (time multiplication factor) in the transference of signals between primary afferent neurons and 2nd order neurons at solitary tract nuclei.

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REFERENCES

ADAMS WE (1958) The Comparative Morphology of the Carotid Body and Carotid Sinus. Springfield, IL: Thomas. 272 pp

ALCAYAGA J, ITURRIAGA R, ZAPATA P (1996) Coherence of chemosensory discharges in cats' carotid nerves. Cooperative inputs or redundant afferences. Adv Exp Med Biol 410: 349-356

BERGER AJ (1979) Distribution of carotid sinus nerve afferent fibers to solitary tract nuclei of the cat using transganglionic transport of horseradish peroxidase. Neurosci Lett 14: 153-158

BERGER AJ, MITCHELL RAM (1976) Lateralized phrenic nerve responses to stimulating respiratory afferents in the cat. Am J Physiol 230: 1314-1320

CHRISTAKOS CN (1994) Analysis of synchrony (correlations) in neural populations by means of unit-to-aggregate coherence computations. Neuroscience 58: 43-57

CIRIELLO J, HRYCYSHYN AW, CALARESU FR (1981) Horseradish peroxidase study of brain stem projections of carotid sinus and aortic depressor nerves in the cat. J Auton Nerv Syst 4: 43-61

CRAGG PA, KHRISANAPANT W (1994) Is the second carotid body redundant? Adv Exp Med Biol 360: 297-299

CROUCH JE (1969) Text-Atlas of Cat Anatomy. Philadelphia, PA: Lea & Febiger. pp 206-207

DE CASTRO F (1928) Sur la structure et l'innervation du sinus carotidien de l'homme at des mammifères. Nouveaux faits sur l'innervation et la fonction du glomus caroticum. Études anatomiques et physiologiques. Trab Lab Invest Biol Univ Madrid 25: 331-380

ELDRIDGE FL, GILL-KUMAR P, MILLHORN DE (1981) Input-output relationships of central neural circuits involved in respiration in cats. J Physiol, London 311: 81-95

EUGENIN J, LARRAIN C, ZAPATA P (1989) Correlative contribution of carotid and aortic afferences to the ventilatory chemosensory drive in steady-state normoxia and to the ventilatory chemoreflexes induced by transient hypoxia. Arch Biol Med Exp 22: 395-408

EUGENIN J, LARRAIN C, ZAPATA P (1990) Functional recovery of the ventilatory chemoreflexes after partial chronic denervation of the nucleus tractus solitarius. Brain Res 523: 263-272

FELDER RB, HEESCH CM (1987) Interactions in nucleus tractus solitarius between right and left carotid sinus nerves. Am J Physiol 253: H1127-H1135

FITZGERALD RS (1976) Single fiber chemoreceptor responses of carotid and aortic bodies. In: PAINTAL AS (ed) Morphology and Mechanisms of Chemoreceptors. Delhi: Patel Chest Inst. pp 27-35

GERSTEIN GL, PERKEL DH, DAYHOFF JE (1985) Cooperative firing activity in simultaneously recorded populations of neurons: detection and measurement. J Neurosci 5: 881-889

GOODMAN NW (1974) Some observations on the homogeneity of response of single chemoreceptor fibres. Respir Physiol 20: 271-281

McQUEEN DS, UNGAR A (1971) On the direct and crossed components of reflex responses to unilateral stimulation of the carotid body chemoreceptors in the dog. J Physiol, London 219: 1-16

NOMURA S, MIZUNO N (1982) Central distribution of afferent and efferent components of the glossopharyngeal nerve: an HRP study in the cat. Brain Res 236: 1-13

PANNETON WM, LOEWY AD (1980) Projections of the carotid sinus nerve to the nucleus of the solitary tract in the cat. Brain Res 191: 239-244

PERKEL DH, BULLOCK TH (1968) Neural coding. A report based on an NRP work session. Neurosci Res Program Bull 6: 221-348

SEIDERS EP, STUESSE SL (1984) A horseradish peroxidase investigation of carotid sinus nerve components in the rat. Neurosci Lett 46: 13-18

SERANI A, LAVADOS M, ZAPATA P (1983) Cardiovascular responses to hypoxia in the spontaneously breathing cat: reflexes originating from carotid and aortic bodies. Arch Biol Med Exp 16: 29-41

WU J-Y, TSAU Y, HOPP H-P, COHEN LB, TANG AC, FALK CX (1994) Consistency in nervous systems: trial-to-trial and animal-to-animal variations in the responses to repeated applications of a sensory stimulus in *Aplysia*. J Neurosci 14: 1366-1384

ZAPATA P, ZUAZO A (1980) Respiratory effects of dopamine-induced inhibition of chemosensory inflow. Respir Physiol 40: 79-92

ZAPATA P, HESS A, BLISS EL, EYZAGUIRRE C (1969) Chemical, electron microscopic and physiological observations on the role of catecholamines in the carotid body. Brain Res 14: 473-496