PHYSIOLOGY

Chronotropic and Inotropic Components of Cardiac Reflexes in Cats

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The relationship between chronotropic and inotropic components of cardiac reflexes were studied in cats using intravenous blood injections, occlusion of the abdominal aorta, pressing on eyeballs (Aschner maneuver), and occlusion of the carotid arteries. Inotropic reactions were characterized by the contractility index DP×HR/MSAP. Different reflexes were shown to be characterized by different ratio of chronotropic and inotropic components, in addition, heart rate and contractility were often altered in opposite directions.

Key Words: *heart; nervous control; chronotropic influences; inotropic influences*

Anatomical background for separate nervous influences on the rate and force of heart contractions are known from the end of XIX century. Parasympathetic innervation of the sinus node was proved to be much more represented than in ventricles, and sympathetic innervation of ventricles, alternatively, is extensive, moreover, right sympathetic nerve innervates both the sinus node and the ventricles, while the left one innervates primarily the ventricles. However, separate innervation of sinus node and ventricles does not allow to estimate whether it is employed for independent regulation of rate and force of heart contractions under normal conditions or not. Meanwhile, relationship between inotropic and chronotropic components of cardiac reflexes was studied only in few studies, where sufficiently reliable characteristics of nervous inotropic influences were not employed. Investigation of this relationship appeared to be the aim of this study.

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MATERIALS AND METHODS

Sixty acute experiments were carried out on adult cats of both sexes under pentobarbital anesthesia: initial dose 60 mg/kg intraperitoneally, maintaining dose 20 mg/kg/h through an intravenous catheter. Permanent infusion of Ringer—Locke solution with rheopolyglucin and heparin was provided though another catheter to maintain the diastolic blood pressure at the level >50 mm Hg. For blood pressure registration, an Elema-Shonander transducer connected with a catheter was introduced into the brachial artery. ECG was recorded by a P4Ch-02 polygraph. Following thoracotomy during artificial lung ventilation a catheter coupled with pressure transducer Statham P34XL (measurement frequency >300 Hz) was introduced into left ventricle. In some experiments, a hook-shaped electrode was applied on right atrium to provide electric stimulation with frequency slightly exceeding the natural heart rate. The loop for abdominal aorta occlusion was applied through 2 cm abdominal incision. Digitized signals were grabbed by a computer (sampling rate 1 kHz). The contractility index (DP×HR/MSAP), which is optimal for assessment of inotropic influences [1], was calculated. The following stimuli were applied: 1) intravenous infusion of 10-20 ml blood (preliminary collected from the same animal; 2) occlusion of the abdominal aorta; 3) eyeball pressing for 1 min (Aschner maneuver); 4) bilateral carotid artery occlusion. The relationship between the chronotropic and inotropic components was assessed using the ratio of unidirectional, differently directed and isolated (when only one parameter had significantly changed) reactions of moment heart rate and DP×HR/MSAP index; the ino-chronotropic ratio (ratio of DP×HR/MSAP index changes (%) and moment heart rate changes (%); absolute value of correlation coefficient between curves of moment heart rate and DP×HR/MSAP index changes. The letter parameter served for the assessment of the dynamics of changes of this parameters. The curves were averaged by 10 points with elimination of accidental and respiratory oscillations; only trends associated with reflex reaction were analyzed.

For statistical analysis Student's test and Pearson's coefficient were used.

RESULTS

Intravenous blood infusion was predominantly associated with negative chronotropic and inotropic effects. Positive effects were less common. In addition, positive inotropic effects occurred 3 times higher, than positive chronotropic effects (Table 1; Fig. 1, *a-c*). Inotropic effects under conditions of forced and intrinsic rhythms were the same (Fig. 1, *a*, *b*). It eliminates the possibility of significant influence of chrono-inotropic relationship in altering the contractility index. Both, positive and negative inotropic effects were more pronounced than the corresponding chronotropic effects (Fig. 2, *a*, *b*). Chronotropic and inotropic effects were unidirectional in 50% observations (Table 2; Fig. 1, *a*), in $^1/_3$ of observations they were differently directed (Fig. 1, *c*); other observations included isolated chronotropic and inotropic effects. Ino-chronotropic ratio was 1.3, which indicated a significant prevalence of inotropic component over the chronotropic one (Fig. 3, *a*). Dynamics of both effects appeared to be similar, which was seen from coefficient of correlation of 0.56 (Fig. 3, *e*).

Occlusion of the abdominal aorta was associated with negative and positive chronotropic effects in the same number of observations; similar picture was observed for inotropic effects (Table 1, Fig. 1, *d-f*). Inotropic effects under conditions of forced and intrinsic rhythms were the same (Fig. 1, *d*, *e*). Inotropic effects were more pronounced than chronotropic (Fig. 2, *c*, *d*). Chronotropic and inotropic effects were unidirectional in 59.2% observations (Fig. 1, *d*), and they were differently directed in 19.2% observations (Fig. 1, *f*), the rest observations included isolated chronotropic and inotropic effects (Table 2). Ino-chronotropic ratio was 1.18, and the coefficient of correlation was 0.65 (Fig. 3, *b, f*).

Pressing on eyeballs was associated with negative and positive chronotropic effects in the same number of observations; insignificant chronotropic effects comprised less than 7% (Table 1, Fig. 1, *g-i*). Pattern of inotropic effects was significantly differed from that of chronotropic effects by the prevalence of positive effects (more than 50%) and greater amount of insignificant responses ($^1/_3$ from all observations). Inotropic effects under conditions of forced and intrinsic rhythms were the same (Fig. 1, *g*, *h*). Both, chronotropic and inotropic responses were less pronounced than after other stimulations (Fig. 2, *e*, *f*). Ratios of unidirectional and differently directed effects were the same, $^1/_4$ of observations included isolated chronotropic effects (Table 2). Ino-chronotropic ratio was 1.04, which indicated only a slight prevalence of inotropic component over chronotropic one (Fig. 3, *c*). Coefficient of correlation was 0.51 (Fig. 3, *g*).

After occlusion of the carotid arteries, the chronotropic responses were often negative and inotropic responses were commonly positive (Table 1; Fig. 1, *j-l*). Inotropic effects under conditions of forced and intrinsic rhythms were the same (Fig. 1,

TABLE 1. Chronotropic and Inotropic Components of Cardiac Reflexes (*M*±*m*; %)

Stimulus	Chronotropic response			Inotropic response		
	-	+	0	-	+	0
Intravenous blood infusion (*n*=71)	74.5±5.2	12.7±3.9	12.7±3.9	56.7±6.1	38.8±6.0	4.5±2.5
Occlusion of abdominal aorta (*n*=122)	40.20±4.44	40.20±4.44	19.7±3.6	45.70±4.63	45.70±4.63	8.6±2.6
Aschner maneuver (*n*=15)	46.7±12.9	46.7±12.9	6.7±6.5	13.3±8.8	53.3±12.9	33.3±12.2
Occlusion of carotid arteries (*n*=25)	60.0±9.9	36.0±9.6	4.0±3.9	32.0±9.3	56.0±9.9	12.0±6.5

Note. *n* — number of responses; "-" — negative response; "+" — positive response; "0" — insignificant effect.

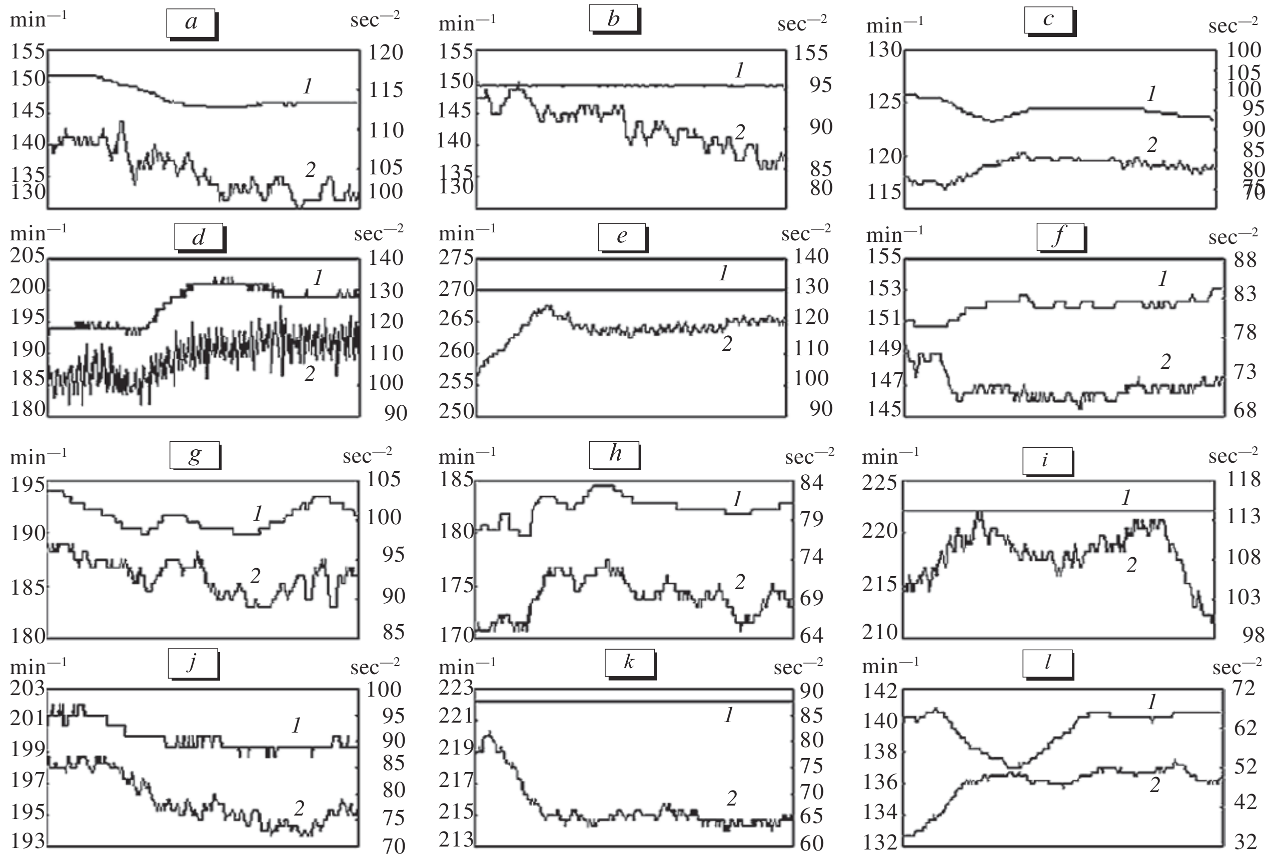

Fig. 1. Changes in heart rate and heart force after reflexogenic stimuli. *a-c*: intravenous blood infusion; *d-f*) occlusion of the abdominal aorta; *g-i*) Aschner maneuver; *j-l*) occlusion of the carotid arteries. *1*) momentary heart rate; *2*) contractility index DP×HR/MSAP. Left vertical axis: moment heart rate values; right vertical axis: index DP×HR/MSAP values.

j, *k*). Both, positive and negative inotropic effects were more pronounced than relevant chronotropic responses (Fig. 2, *g*, *h*). The responses were unidirectional almost in half of observations (Fig. 1, *j*), half as less frequent they were differently directed (Fig. 1, *l*), isolated chronotropic (12%) and inotropic (4%) responses were even less common (Table 2). Ino-chronotropic ratio was 1.09, and the coefficient of correlation was 0.56 (Fig. 3, *d*, *h*).

Thus, each reflex was characterized by a unique relationship between the chronotropic and inotropic components. For example, Aschner maneuver was associated more frequently with chronotropic effects than with inotropic ones, and if both types of responses occurred, the inotropic component hardly ever prevailed over the chronotropic one, in contradistinction from another stimuli, (ino-chronotropic ratio was 1.04). Aschner maneuver appeared to be the "most chronotropic" among all investigated stimuli. Alternatively, intravenous blood infusion was associated with the most pronounced prevalence of inotropic component (ino-chrono-

TABLE 2. Relationship Between Chronotropic and Inotropic Components of Cardiac Reflexes (*M*±*m*; %)

Stimulus	Responses			
	inudirected	differently directed	isolated	
			chronotropic	inotropic
Intravenous blood infusion	49.3±6.1	32.8±5.7	4.5±2.5	13.4±4.2
Occlusion of abdominal aorta	59.2±4.5	19.2±3.6	5.0±2.0	16.7±3.4
Aschner maneuver	37.5±12.1	37.5±12.1	25.0±10.8	0
Occlusion of carotid arteries	56.0±9.9	28.0±9.0	12.0±6.5	4.0±3.9

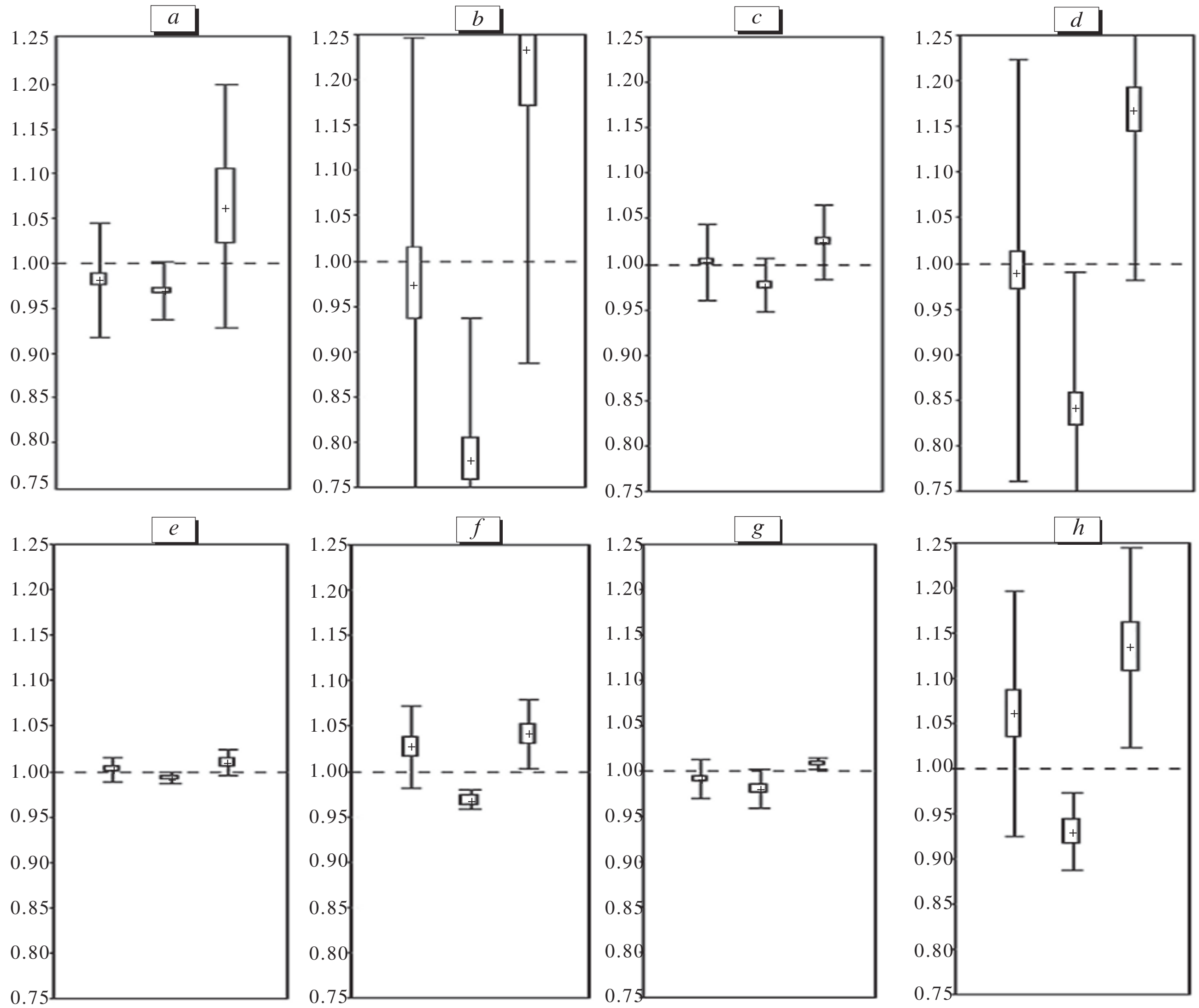

Fig. 2. Chronotropic and inotropic components of cardiac reflexes in cats. Changes (in % from background value) in momentary heart rate (*a*, *c*, *e*, *g*) and contractility index DP×HR/MSAP (*b*, *d*, *f*, *h*) after reflexogenic stimuli. In each group: 1st bar — for all responses; 2nd bar — for negative responses; 3rd — for positive responses. *a*, *b*) intravenous blood infusion; *c*, *d*) occlusion of the abdominal aorta; *e*, *f*) Aschner maneuver; *g*, *h*) occlusion of the carotid arteries.

tropic ratio was 1.3), and isolated inotropic effect appeared effect after this stimulus occurred 3 times as frequent isolated chronotropic one; thus, response after intravenous blood infusion appeared to be the "most inotropic".

The rate of differently directed reactions was unexpectedly high ($^1/_4$ of all reflex responses, reaching 37.5% after Aschner maneuver). This raises the question concerning physiological significance of such independent regulation of heart rate and heart force. One might think that chronotropic and inotropic influences in the context of cardiac output are equivalent and always have to be undirected and paralleled. However, consequences of changes in heart rate and contractility are different. For example, heart rate affected cardiac output not only directly, but also indirectly, trough altering the filling of the heart. At high heart rate, when the slow filling purse disappears, the increase in heart rate leads to shortening of rapid filling phase, to reduction of end-diastolic volume, and as a consequence, to reduction of stroke volume. In addition, since the coronary blood flow is provided generally in diastole, the increase in heart rate and shortening of diastole is associated with impairment of heart blood flow. On this account positive inotropic effect is associated with more pronounced improvement coronary blood flows, than positive chronotropic effect [4]. Combination of positive inotropic response (to make a heart to trough out whole amount of influent blood) and negative chronotropic effect (to prolong the diastole for appropriate filling of the

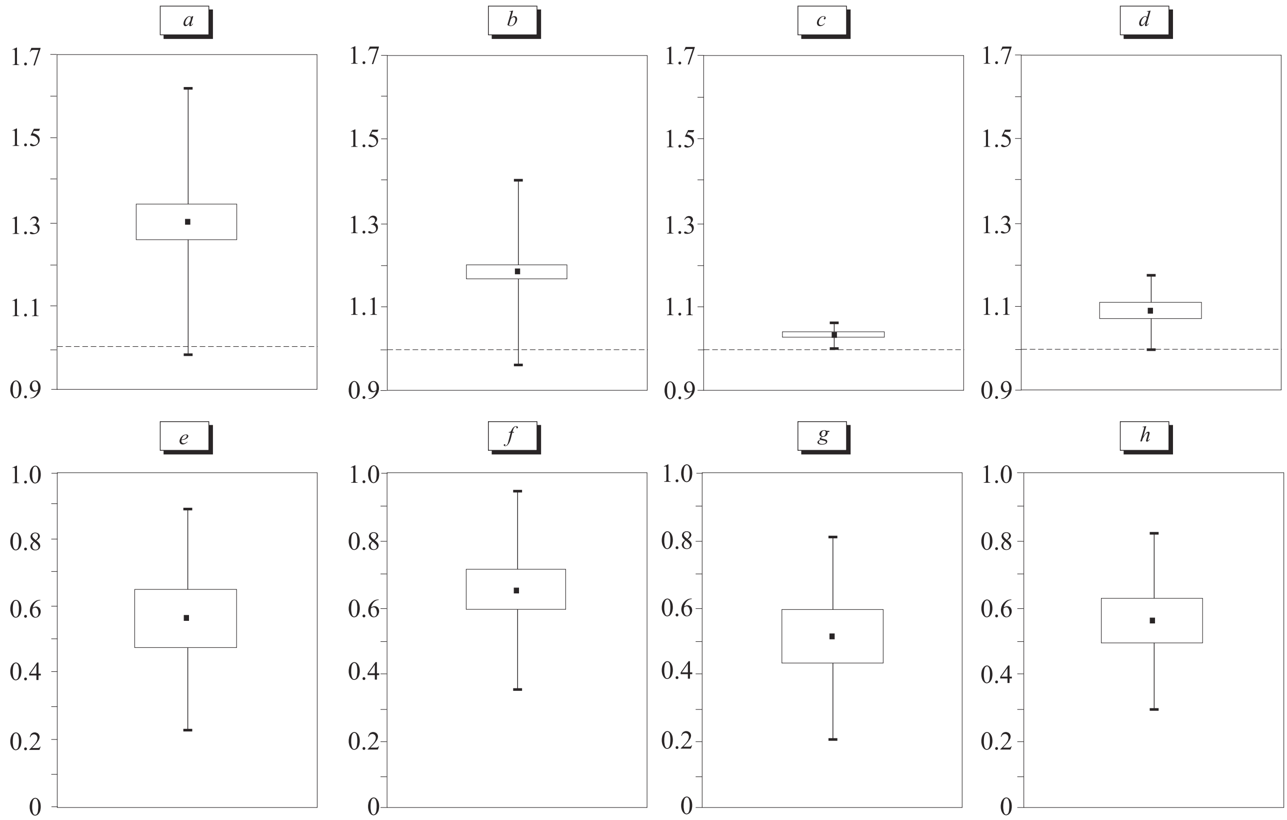

Fig. 3. Relationship between chronotropic and inotropic components of different cardiac reflexes in cats. *a-d*) ino-chronotropic ratio; *e-h*) absolute value of correlation coefficient between curves of momentary heart rate and DP×HR/MSAP index changes. *a*, *e*) intravenous blood infusion; *b*, *f*) occlusion of the abdominal aorta; *c*, *g*) Aschner maneuver; *d*, *h*) occlusion of the carotid arteries.

heart) can be assumed to be useful under conditions of increased venous return and initially high heart rate. This can explain the high rate of differently directed chrono- and inotropic reactions after intravenous blood infusion. Non-parallel changes in stroke volume and heart rate are well-known in sports medicine [3].

Coefficient of correlation between changes in moment heart rate and DP×HR/MSAP index varied from 0.51 to 0.65 for different reflexes. Previously, during the investigation of chrono-dromotropic coordination in cats the coefficient of correlation obtained between changes in RR and AB interval values was 0.28-0.53 [2]., *i.e.* the dynamics of inotropic and chronotropic responses are more similar, than those for inotropic and dromotropic effects. At first glance, it may seem extraordinary: sinus and antrioventricular nodes are closer to each other, than to myocardium in the respect of tissue origin, physiological properties, and regulation mechanisms. Fast, quick-response regulation, indicative for those nodes, is predominantly provided by "fast" parasympathetic system, what allows the modification of heart rate and atrioventricular delay within one cardiac cycle (by the cycle regulation). Alternatively, cardiac muscle is characterized by slow, delayed-action regulation, predominantly provided by "slow" sympathetic system. The development and extinction of its reactions takes several minutes. One might expect the dynamics of chronotropic and dromotropic effects to be even not the same but more similar, than those for chronotropic and inotropic effects. However, we obtained alternative results indicating the dependence of the response type not from whether it mediated by sympathetic or parasympathetic system, but from the coordination of nervous influences, involving both departments of the autonomic nervous system to form the optimal pattern of heart activity.

REFERENCES

1. N. N.Alipov, O. V. Sergeeva, N. A. Bobrova *et al., Bull. Exp. Biol. Med.*, **145**, No. 2, 127-132 (2008).
2. N. N. Alipov, A. V. Sokolov, L. V. Trubetskaya, and T. E. Kuznetsova, *Bull. Exp. Biol. Med.*, **132**, No. 12, 616-620 (2001).
3. A. G. Dembo and E. V. Zemtsovskiy, *Sports Cardiology* [in Russian], Leningrad (1989).
4. R. D. Janes, D. E. Johnstone, and J. A. Armour, *Can. J. Physiol. Pharmacol.*, **62**, No. 11, 1374-1381 (1984).