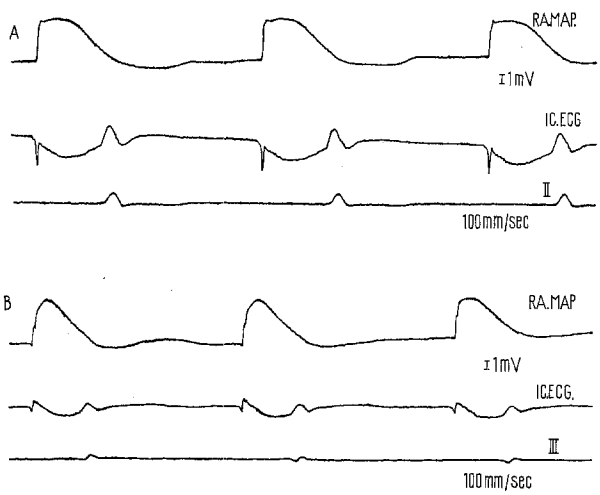
The Effect of Thyroid State on Monophasic Action Potential in Human Heart

Hyperthyroidism is a common cause of supraventricular arrhythmias, whereas in myxoedema irregularities of cardiac rhythm are rare. The direct effect of differences in thyroid state on cardiac intracellular potentials were studied by FREEDBERG et al.[1], showing that the duration of the repolarization phase of the action potential was greatly prolonged in atria from thyroidectomized rabbits, and was shortened in hyperthyroid atria. These changes being in relation with the duration of the atrial muscle refractoriness, could account for a reduced probability of arrhythmias in hypothyroidism.

Intracardiac recording of the monophasic action potential (MAP) in the intact human heart, using a suction electrode technique, offers new possibility to obtain indications about the electrical activity of the myocardium. The MAP recorded in this way may be taken as a reliable index of the shape of the action potential during the entire phase of repolarization[2,3]. The recording of the MAP by the suction electrode technique is obtained from a great number of cells, therefore it does not represent the true transmembrane potential. Nevertheless its duration is an important parameter which expresses the refractoriness of the atrial myocardium, an important determinant of the nature of response to a given stimulus[2,4].



Monophasic action potential of the right atrium (RAMAP) recorded simultaneously with an intracavitary electrocardiogram (ICECG) and one standard ECG lead, in patient No. 3, from Table I. A) Before treatment. The mean duration of monophasic action potential measured at 90% of the amplitude is 330 msec. B) After 2 weeks of treatment with thyroid hormone. The mean duration of the monophasic action potential shortened to 240 msec.

We have used for the MAP recording a simple bedside suction technique, with bipolar electrode catheters, introduced percutaneously, and positioned through continuous monitoring of the intra-cavitary electrocardiogram, without X-rays control. The recordings were picked up on a 6 channel recorder, using a paper speed of 50 or 100 mm/sec and the amplitude was adapted by changing the etalon for each determination, in order to have a good curve of the MAP.

Such MAP recordings were done in 9 patients, 7 with hypothyroidism and 2 with hyperthyroidism. In 4 patients with hypothyroidism the MAP was recorded also after 2 weeks of treatment with thyroid hormone (Table I).

Between the patients in hypothyroid state (Table I), and those with hyperthyroidism (Table II) an evident difference appears concerning the duration of the MAP and also the rate of rise of the action potential during phase three of the repolarization (dV/dt 3).

In the 4 patients with myxoedema in whom the MAP was recorded before and after treatment with thyroid hormone, we have found a significant shortening of the MAP duration in the second determination (Table I). The duration measured at 50% of the amplitude was also shortened, but no big differences were observed on dV/dt 3. In the Figure we present the MAP recorded in patient No. 3 from Table I, before (A), and after (B) 2 weeks of treatment with thyroid hormone (125 mg/day). At the almost same heart rate the differences in the MAP curves can be observed (Figure).

Our findings are in complet agreement with the experimental data obtained by FREEDBERG, underlining the influence of thyroid state on the duration of the action potential through the metabolic changes induced in the cardiac muscle. This prolonged duration of the MAP, showing

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[3] B. OLSSON, in *Symposium on Cardiac Arrhythmias*, Elsinore, Danmark 1970 (AB Astra, Södertälje, Sweden), p. 37.
[4] E. M. VAUGHAN, in *Symposium on Cardiac Arrhythmias*, Elsinore, Danmark 1970 (AB Astra, Södertälje, Sweden), p. 449.

Table I. The MAP caracteristics in 7 patients with hypothyroidism

No.	Name	Sex	Age	RA MAP before treatment						RA MAP after thyroid treatment					
				P-P	A	D_1	D_2	D_3	dV/dt 3	P-P	A	D_1	D_2	D_3	dV/dt 3
1	CA	♀	48	900	5	390	330	180	380	660	5	340	300	170	390
2	MS	♀	48	720	3.5	300	230	160	400	600	3.4	240	220	150	544
3	SB	♀	43	940	4.2	340	300	230	450	880	4.2	270	240	170	500
4	CM	♀	54	950	4.5	380	330	190	360	900	4.6	300	230	170	520
5	CT	♂	64	780	4.4	390	360	280	365						
6	GI	♂	58	750	5	400	360	270	178						
7	HA	♀	44	760	5	400	350	300	388						

Abbreviations: P-P, P-P interval in msec; A, amplitude in mV; D, duration measured at isoelectric line; D_2, duration at 90% of the amplitude; D_3, duration at 50% of the amplitude; dV/dt 3, the rate of rise of the action potential during phase 3; RA MAP, right atrium monophasic action potential.

an increase of the atrial muscle refractoriness, may explaine the rarety of atrial arrhythmias in hypothyroidism comparatively with hyperthyroidism, and provides clues to understand the underground of the rhythm disturbances[1,4].

Table II. The MAP caracteristics in 2 patients with hyperthyroidism

No.	Name	Sex	Age	P-P	A	D_1	D_2	D_3	dV/dt 3
1	SE	♀	53	580	4.5	230	170	110	1150
2	GT	♀	60	620	4	240	200	140	820

Résumé. L'enregistrement du potentiel monophasique d'action de l'auricule droite a été effectué à l'aide des électrodes de succion, chez 9 patients. On constate un allongement notable du potentiel monophasique chez les hypothyroïdiens, il se raccourcit après traitement thyroïdien, tandis que chez les hyperthyroïdiens sa durée est diminuée.

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Identification of Temperature Increases and Decreases: A Difficult Task for Monkey and Human[1]

Many authors have subdivided somatosensation into 4 sub-modalities of sensory experience-tactile, cool, warm and pain[2–4]. Based on this consensus, attempts were made to train 2 monkeys to discriminate tactile, cool and painfully hot stimuli delivered separately in time to the same area on the shaved dorsal surface of the rigidly held forearm (Figure). The monkeys were required to make discriminations by pressing the appropriate one of 3 available levers when the stimulus came on (Figure 1A).

Although the monkeys learned to discriminate the tactile and thermal stimuli, they did not learn to discriminate the 2 thermal stimuli. Numerous changes in training procedures made over a 2 years period were inadequate in establishing the discrimination. There are several possible explanations for this failure: 1. the correct training contingencies were not used. 2. The triple discrimination task was beyond the monkey's 'intellectual' capacity. 3. The rates of change of the thermal stimuli were too slow. 4. Monkeys do not have the sensory capacity to discriminate temperature increase from decreases as they were applied in this experiment.

When an auditory stimulus was substituted for the cool stimulus, the monkeys learned to discriminate the auditory from the hot and tactile stimuli, thereby eliminating both the first and second explanations. When the rate of change of the thermal stimuli was increased (Figure 1C), the monkey was still unable to learn the discrimination, thereby making the 3rd explanation less likely. To test the 4th explanation further, 12 naive humans were tested with the same apparatus. Although all subjects were able to detect the presence of a thermal stimulus, they also reported difficulty in identifying the 'quality' (i.e. direction of change) of that thermal stimulus. The human subjects, therefore, made errors in lever press responses much like the monkey subjects. Most human subjects developed these difficulties after the testing began, usually within 5 to 20 min, but 3 subjects reported confusion on the first trial (Table, compare first and last 4 trials).

Although these discrimination difficulties appear to be related to the phenomenon of paradoxical cold, this phenomenon occurs rarely and only with pinpoint stimuli which are normally easy to identify[5,6]. Furthermore, most of the errors made by the human subject in this experiment were identifying the cool stimuli as 'hot', thereby suggesting the errors be described as 'paradoxical hot', a phenomenon even more rarely reported. It seems reasonable to conclude, therefore, that it was difficult to train monkeys to discriminate the hot and cool stimuli because, like humans, the monkey does not have the sensory capacity for such discrimination under these conditions. This conclusion is surprising because, phenomenologically, hot and cool seem easy to identify. It remains to be determined what characteristics of this experimental situation make the identifications so difficult.

There are several possibilities. It is possible that the stimulus parameters were not changed appropriately to effect the identification of hot and cool. KENSHALO et al.[7] have found that it takes a larger temperature change to produce identification of cool or warm than it does to produce a simple detection of change, especially at the adapting temperature used in this experiment (37.7°C). A possibly immoderate adapting temperature is not the complete explanation, however, because the amounts of change required for identification of cool and warm at 37–38°C in the KENSHALO et al. experiment[7] (1–1.5°) were much smaller than those used in this experiment (Figure 1C).

Another possibility is the occurrence of both hot and cool stimuli within the same testing session. The fact that some of the human subjects made identification errors on the first trial, however, tends to negate this possibility.

Other possibilities include the size and locus of the stimuli. Stimulus size is not probable because the stimulator used here was larger than the range over which areal summation occurs[8–10]. Locus, however, may be important,

[1] Supported in part by grants PHS MH 11218, NB 7468, NS 92992 and NSF GU 2612.

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