gradient centrifugation'' using ^{14}C-labeled Δ^9-THC (specific activity: 10.5 mCi/mmole). If the low specific activity Δ^9-[^{14}C]THC sedimenting at ''10.4*S*'' in their assay were indeed bound to estrogen receptor as claimed (*6*), the concentration of receptor sites would greatly exceed 100,000 fmole per milligram of cytosol protein (compared with the few hundred femtomoles per milligram usually detected in uterine cytosol).

Evidence from bioassays in vivo also is weighted strongly against any direct estrogenic action by cannabinoids. Several reports on various species have shown that Δ^9-THC and other cannabis preparations either exert antiestrogenic effects (*2, 4*) or are without effect on the uterus. The authors of the two reports (*11*) claiming that Δ^9-THC has estrogenic actions on the uterus and vagina used only 21 rats treated with Δ^9-THC and indicated that a very moderate ''estrogenic'' response appeared to occur only in seven rats injected with 2.5 mg/kg doses of Δ^9-THC.

The fact that high doses of cannabinoids can alter reproductive tissues in experimental animals is unquestioned. The reproductive effects in humans are unclear. In either case it is unlikely that any reproductive alterations are due to the direct estrogenic activity of Δ^9-THC.

ALLAN B. OKEY, GREGORY P. BONDY
Department of Biology, University of Windsor, Windsor, Ontario N9B 3P4

References and Notes

1. R. Collu, J. Letarte, G. Leboeuf, J. R. Ducharme, *Life Sci.* **16**, 553 (1975); V. P. Dixit, V. N. Sharma, N. K. Lohiya, *Eur. J. Pharmacol.* **26**, 111 (1974); M. E. Corcoran *et al.*, *Res. Commun. Chem. Pathol. Pharmacol.* 7, 779 (1974).
2. I. Chakrabarty, D. Sengupta, P. Bhattacharya, J. Ghosh, *Biochem. Pharmacol.* **25**, 377 (1976); V. P. Dixit, M. Arya, N. K. Lohiya, *Endokrinologie* **66**, 365 (1975); I. Chakravarty, D. Sengupta, P. Bhattacharya, J. J. Ghosh, *Toxicol. Appl. Pharmacol.* **34**, 513 (1975); G. R. Thompson, M. M. Mason, H. Rosenkrantz, M. C. Braude, *ibid.* **25**, 373 (1973).
3. R. C. Kolodny, W. H. Masters, R. M. Kolodner, G. Toro, *N. Engl. J. Med.* **290**, 872 (1974); J. Harmon and M. A. Aliapoulios, *ibid.* **287**, 936 (1972); J. H. Mendelson, J. Kuehnle, J. Ellingboe, T. F. Baber, *ibid.* **291**, 1051 (1974).
4. A. B. Okey and G. S. Truant, *Life Sci.* **17**, 1113 (1975).
5. A. B. Okey and G. P. Bondy, *Science* **195**, 904 (1977).
6. A. B. Rawitch, G. S. Schultz, K. E. Ebner, R. M. Vardaris, *ibid.* **197**, 1189 (1977).
7. Cytosol becomes turbid when 1 m*M* concentrations of Δ^9-THC are added but clarifies during overnight shaking. The true initial concentration of Δ^9-THC in solution probably does not exceed 10 μM.
8. G. C. Chamness and W. L. McGuire, *Steroids* **26**, 538 (1975).
9. G. P. Bondy, A. B. Okey, W.-L. Kuo, unpublished observations.
10. The [^{14}C]formaldehyde-labeled BSA used in each sample tube is at a concentration well below 1 μg/ml; thus, binding at the 4- to 5*S* peak for ^{3}H-labeled Δ^9-THC is not to the marker protein.
11. J. Solomon, M. A. Cocchia, R. Gray, D. Shattuck, A. Vossmer, *Science* **192**, 559 (1976); J. Solomon, M. A. Cocchia, R. DiMartino, *ibid.* **195**, 875 (1977).
12. G. M. Stancel and J. Gorski, in *Methods in Enzymology*, B. W. O'Malley and J. G. Hardman, Eds. (Academic Press, New York, 1975), p. 166.
13. J. L. Wittliff, in *Methods in Cancer Research*, H. Busch, Ed. (Academic Press, New York, 1975), p. 293.
14. The Δ^9-THC, Δ^8-THC, and 11-hydroxy-Δ^9-THC were supplied through the courtesy of R. A. Graham, Health Protection Branch, Health and Welfare Canada. Supported by a grant from the National Research Council of Canada.

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Activity Patterns of Human Skeletal Muscles: Relation to Muscle Fiber Type Composition

Abstract. *The muscle activity of normal ambulatory individuals was recorded continuously for 8-hour (working day) periods. Parameters of activity patterns were defined and numerical outcomes for these parameters were compared across a diverse population of muscles. Several pattern parameters, such as the average percentage of time active, were highly correlated with the percentage of type I fibers of a muscle.*

Mammalian skeletal muscles can be classified in a number of ways (*1*). Historically, classification has been based on gross muscle characteristics, such as vascularity, and on the average contraction time of the twitch response. More recent histochemical methods show that mammalian skeletal muscles are composed of metabolically diverse fibers (*2, 3*). Two main muscle fiber types (''archetypes'' I and II) have been defined as a function of both histochemical and physiological measures (*4*).

Metabolic profiles of mammalian skeletal muscles, based either on fiber type composition alone or on more complex classification schemes, differ. There is increasing evidence that profile differences reflect differences in normal functional muscle use. At least a limited adaptive range exists, since several enzyme systems have been shown to gradually adapt to changes in functional demand (*5, 6*). However, it remains to be established what specific physiological factors (such as average speed of movement) modulate what aspects of the metabolic profile (such as enzyme systems). In the study reported here we define a number of parameters of normal activity patterns. Several of these parameters are highly correlated with the muscle's fiber type composition. In contrast to most previous approaches, in which the activity pattern of a single muscle was manipulated experimentally and profile changes were observed in time by sequential sampling, our approach involves a comparison between defined parameters of naturally occurring patterns and profiles, for a diverse population of human muscles. This acknowledges that the intrinsic properties of a muscle's motoneuron pool, such as the synaptic organization of its input and the distribution of cell sizes, affect a muscle's activity pattern in a specific manner.

Muscle usage patterns of 12 normal males between the ages of 20 and 35 years were recorded continuously over 8-hour (working day) periods (9 a.m. to 5 p.m.). These individuals were either hospital employees (N = 7) or paid volunteers (N = 5). Muscle usage was based on the electrical activity of the muscle during contraction, recorded on an electromyogram (EMG) (*7*). Recordings were made simultaneously from two functionally linked (*8*) but histochemically different muscles. The analysis of pattern parameters, such as percentage of time active, could thus be normalized for variations in day-to-day usage by only considering relative differences in outcome between the two paired muscles. There were no restrictions on the types of activities that individuals could engage in, but some experimental variables were controlled in the recording of specific muscles [for example, heel height, which affects the relative use of ankle flexors and extensors during quiet standing (*9*)]. Activity patterns were recorded with a pocket-size tape recorder (*10*), which ensured unobtrusive data collection and did not encumber the individual. Tapes were reproduced at 60 times the recording speed. Parameters of each reproduced pattern were analyzed by computerized scanning of the rectified and smoothed electromyogram (|EMG|) (*11*).

Selection of the population of muscles was influenced by the availability of comparative data on metabolic profiles of human skeletal muscles. The available data apply to a variety of species and were obtained by a number of histochemical methods. For consistency, histochemical data were taken from a single study (*12, 13*) in which multiple muscle biopsies were obtained from 36 different muscles of six males in the age range 18 to 30 years. The metabolic profile parameter examined in (*12*) was the percentage of type I fibers, based on the staining density of myofibrillar adenosinetriphosphatase.

The selection of muscles also depend-

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ed on the expected variability of the activity pattern of each muscle over the observation period. Variability is a function of (i) the diversity of stereotyped motor actions that a muscle participates in, (ii) the average repetition rate of these actions relative to the 8-hour period of observation, and (iii) numerous ill-defined effects of environment, vocation, and habits. Several typical motor patterns are shown in Fig. 1A; the top-to-bottom arrangement of the five patterns is based on the percentage of type I fibers that these muscles, on the average, contain [(*12*) see Fig. 2]. Temporal-spatial variability in the usage of each muscle as well as coincidence of activity among muscles is illustrated by plotting levels of activity on a compressed time scale (Fig. 1B). Variability was comparatively low for only one muscle, the palpebral part of the orbicularis oculi (trace A in Fig. 1B). This results from the sustained repetitive nature of the eye blink and the stereotyped |EMG| geometry of each blink (*14*). The consistency of this activity pattern, except for an occasional squint and numerous voluntary adjustments in average blink rate, contrasts with the behavior of all of the other muscles examined. Traces B, C, D, and E of Fig. 1B show the concomitant activity of four leg muscles over a 4-hour period. Note (i) the temporal similarity among the four traces (strong functional linkage, compared to traces F, G, H, and I), (ii) the variability over time within each trace (compared to orbicularis oculi), and (iii) the quantitative differences in the amounts of activity for the two more postural muscles (biceps femoris and tibialis anterior) compared to the more phasic (spikelike) pattern of the gastrocnemius muscle and the very phasic pattern of the rectus femoris muscle. Activity patterns of arm and wrist muscles (traces F, G, H, and I in Fig. 1B) were more phasic than patterns of leg muscles. The antigravity function of some arm muscles (biceps brachii and, to some extent, as when sitting at a desk or a table, the wrist extensors) causes these muscles to be comparatively more active.

The lines in Fig. 2B mark the average percentage of time active over 8 hours for 38 muscle pairs. One data point was obtained for each muscle recording by measuring the total duration of activity that was above threshold, relative to the total time of observation; the data points for the two muscles of a pair were connected by a line. The slopes of the lines in Fig. 2B show that for nearly all pairs the more active muscle contains the higher percentage of type I [fatigue resistant (*4*)] fibers. Although the trend in the slopes is not in itself surprising, its consistency among such a functionally diverse group of muscles is remarkable. Note from (i) the wide spread in the individual data points for each muscle and (ii) the consistency and average trend of the slopes that whereas day-to-day use of a muscle was highly variable, relative levels of activity within pairs were, for most pairs, nearly the same. The latter finding is attributed to the choice of pairs [many pairs consisted of strongly linked leg muscles (*8*)], the long period of observation, and the homogeneity of the subject population. The percentages shown are probably most representative of semisedentary vocations. The estimate of the percentage of type I for the biceps brachii appears to be low, based on the slopes of the biceps' paired relationships to two other muscles [deltoid and triceps brachii; but see (*15*)]. The high percentage of time active of the adductor pollicis resulted from its continuous discharge during some types of grasping, such as holding a steering wheel while driving a car.

The values in Fig. 2B strictly apply only to the lowest-threshold motor units of a muscle. Percentages for higher-threshold units declined with increasing threshold (with increasing |EMG| amplitude) as specified by the |EMG| amplitude distribution of each recording. To test the internal consistency of the data underlying Fig. 2B, an estimate was made of the minimum percentage of time active of the type I fibers in each muscle. These estimates were derived directly from the |EMG| amplitude distributions by (i) equating the |EMG| amplitude (percent-

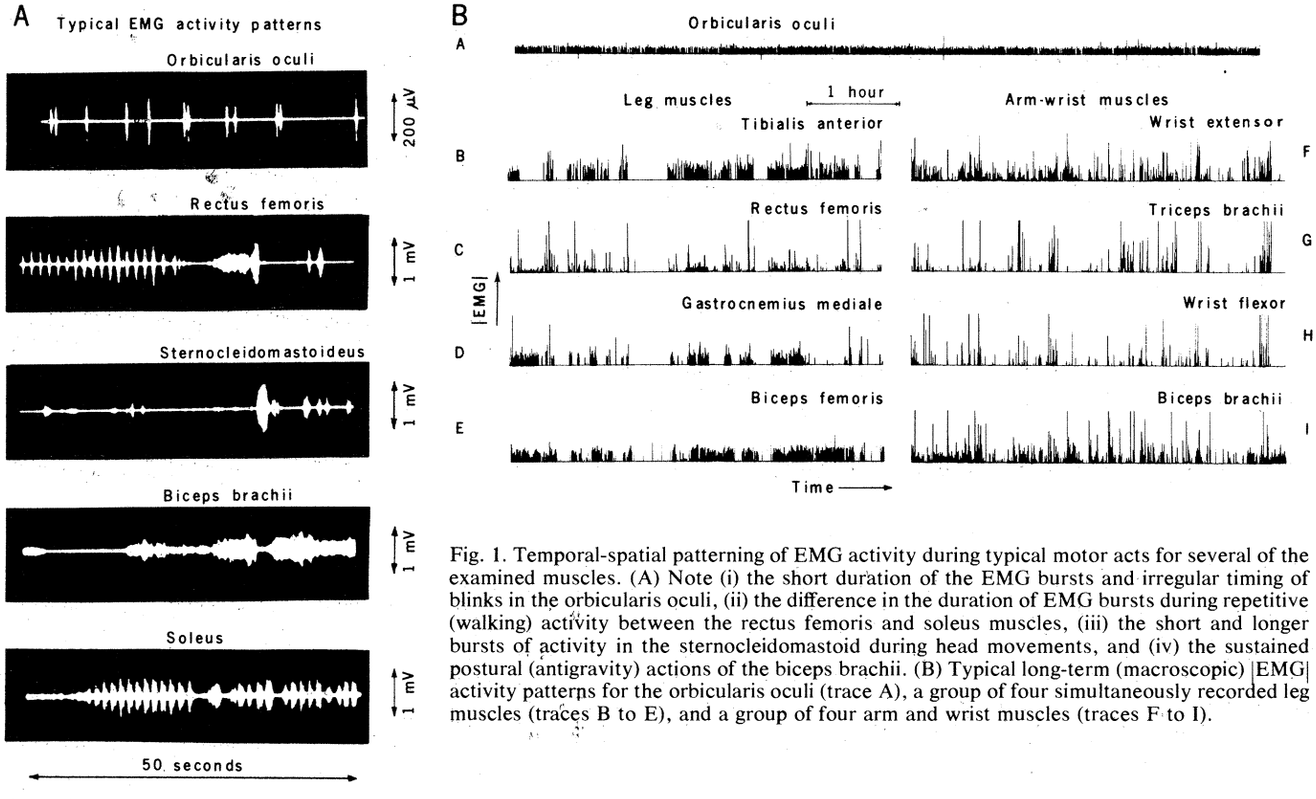

Fig. 1. Temporal-spatial patterning of EMG activity during typical motor acts for several of the examined muscles. (A) Note (i) the short duration of the EMG bursts and irregular timing of blinks in the orbicularis oculi, (ii) the difference in the duration of EMG bursts during repetitive (walking) activity between the rectus femoris and soleus muscles, (iii) the short and longer bursts of activity in the sternocleidomastoid during head movements, and (iv) the sustained postural (antigravity) actions of the biceps brachii. (B) Typical long-term (macroscopic) |EMG| activity patterns for the orbicularis oculi (trace A), a group of four simultaneously recorded leg muscles (traces B to E), and a group of four arm and wrist muscles (traces F to I).

age of maximum) with the percentage of total fibers active, (ii) locating the |EMG| amplitude corresponding to the percentage of type I fibers of the muscle (*12, 13*), and (iii) making a number of assumptions (*16*). It was found that, in contrast to the data in Fig. 2B, the values of percentage of time active for type I fibers were approximately the same for all muscles examined ($> 1.0 \pm 0.7$ percent). This finding thus shows a consistent response of functionally diverse muscles to a specific parameter of normal usage.

There are three ways in which one muscle can have a higher percentage of time active than another: the muscle may be active more frequently (in contractions per unit time), it may remain active for a longer period when it is active (the average on-time per contraction, T_A, may be longer), or both. The mean T_A values and their standard deviations, for all recordings of each muscle combined, are shown in Fig. 2A. The mean T_A values are larger for muscles with a higher percentage of type I fibers. Linear regression of the mean T_A values for each muscle produced the solid line in Fig. 2A, indicating a range from 0.22 to 0.65 seconds. Since (i) the number of contractions per 8-hour period for different muscles was not significantly related to their percentages of type I fibers and (ii) the increases in T_A and percentage of time active were both approximately threefold over the range of muscles examined, the slopes in Fig. 2B result mostly from differences in T_A times (*17*).

It is concluded that the type composition of normal human skeletal muscle can be predicted, within reasonable limits, on the basis of at least two parameters of the normal activity pattern: either the average percentage of time the muscle is active at a specified level or the average on-time per contraction. The observed correlations (Fig. 2) suggest that a general principle, applicable to many, if not all, human skeletal muscles, underlies the relationship between type composition and normal functional usage. However, further analysis is likely to establish other (higher?) correlations with more specific metabolic profile parameters. In this study we did not examine metabolic adaptation per se. However, in light of previous data (*5, 6*), the data obtained suggest that increased usage of a muscle eventually leads to a rise in its percentage of type I fibers and a reduction in its speed of contraction. Further studies should verify the actual adaptive range for muscles exposed to different types of functional demands.

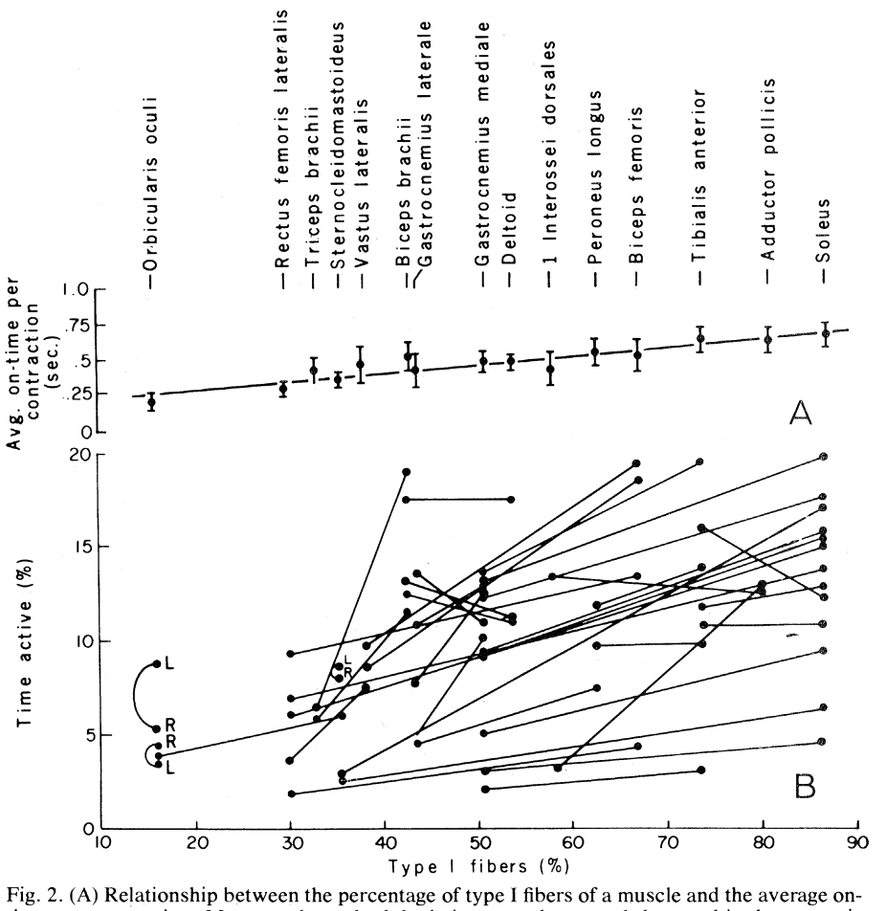

Fig. 2. (A) Relationship between the percentage of type I fibers of a muscle and the average on-time per contraction. Means and standard deviations are shown and the trend in the means is approximated by linear regression (solid line). (B) Percentage of time active of identified muscles, recorded in pairs, again as a function of the percentage of type I fibers of each muscle. The letters *L* and *R* indicate left and right.

A. WILLEM MONSTER
HING C. CHAN, DAVID O'CONNOR
Departments of Rehabilitation Medicine and Physiology, Temple University Health Sciences Center, Philadelphia, Pennsylvania 19140

References and Notes

1. R. I. Close, *Physiol. Rev.* **52**, 129 (1972).
2. F. C. A. Romanul, *Arch. Neurol. (Chicago)* **11**, 355 (1964); S. Schiaffino, V. Hanslikova, S. Pierobon, *J. Cell Biol.* **47**, 107 (1970); V. Dubowitz and N. H. Brooke, *Muscle Biopsy, a Modern Approach* (Saunders, London, 1973).
3. L. Edström and B. Nyström, *Acta Neurol. Scand.* **45**, 257 (1969).
4. A. J. Buller, J. C. Eccles, R. M. Eccles, *J. Physiol. (London)* **150**, 399 (1960); M. H. Brooke and K. K. Kaiser, *Arch. Neurol. (Chicago)* **23**, 369 (1970); J. Barnard, V. R. Edgerton, T. Furukawa, J. B. Peter, *Am. J. Physiol.* **220**, 410 (1971); R. E. Burke and P. Tsairis, *Ann. N.Y. Acad. Sci.* **228**, 145 (1974).
5. W. K. Engel, M. H. Brooke, P. G. Nelson, *Ann. N.Y. Acad. Sci.* **138**, 160 (1966); F. C. A. Romanul and J. P. Van Der Meulen, *Arch. Neurol. (Chicago)* **17**, 387 (1967); S. Salmons and G. Vrbová, *J. Physiol. (London)* **201**, 535 (1969); L. Guth and H. Yellin, *Exp. Neurol.* **31**, 277 (1971); M. Barany and R. J. Close, *J. Physiol. (London)* **213**, 455 (1971); K. M. Baldwin and C. M. Tipton, *Pfluegers Arch.* **334**, 345 (1972); D. Pette, M. E. Smith, H. W. Staudte, *ibid.* **338**, 257 (1973); J. O. Holloszy, *Med. Sci. Sports* **7**, 155 (1975); G. Grimby, C. Broberg, I. Krotkiewska, M. Krotkiewski, *Scand. J. Rehabil. Med.* **8**, 37 (1976).
6. D. A. Riley and E. F. Allin, *Exp. Neurol.* **40**, 391 (1973).
7. Surface (Beckman) as well as intramuscular wire [J. V. Basmajian and G. A. Stecko, *J. Appl. Physiol.* **17**, 849 (1962)] electrodes were used, depending on the size and spatial isolation of the muscle of interest in relation to other nearby muscles. Silver paste (Micro Circuits, Inc.; type SC20) was used for the orbicularis oculi. Muscles combined in pairs were always recorded with the same type of electrode. Several limitations are associated with the use of EMG as a measure of muscle activity. (i) There is preferential sampling of the parts of the muscle that are nearest to the electrode—that is, possible bias toward sampling activity from type II fibers when using surface electrodes (*6, 12*). (ii) The relationship between the EMG amplitude and the contractile state of the muscle is ill-defined, depending on the kinetics of the contraction [O. C. J. Lippold, *J. Physiol. (London)* **117**, 492 (1952); T. W. Calvert, *Proc. IEEE* **65**, 682 (1977)]. (iii) The EMG amplitude scaling is required because the muscles are of different sizes and at different depths and electrode placements vary. For all recordings an empirical scaling method was applied: 90 percent of the cumulative amplitude distribution was scaled to a fixed number; the threshold for "on" relative to "off" was 8 percent of this number for all recordings. (iv) No distinction can be made between EMG changes due to recruitment or derecruitment of motor units and firing rate variations of recruited units (*16*).
8. We originally developed the functional linkage concept to study motor coordination. Strength of linkage is a measure of the extent to which different muscles participate in different phases of specific motor functions. The findings presented here (Fig. 2) do not depend on paired recording; the linkage concept provided a means of reducing experimental variability.
9. J. Joseph and A. Nightingale, *J. Physiol. (London)* **132**, 465 (1956).
10. A two-channel Avionics 445 recorder was used. The bandwidth of this recorder extends to 250 Hz, which is sufficient for recovering most of the power in the EMG signal. The signal-to-noise ratio of the data-handling system was 35 dB, so that noise levels were well under the 8 percent threshold level [item (iii) in (*7*)]. The data in Fig.

1B (traces B to I) were recorded in two groups with a four-channel Medilog (Oxford Instruments) recorder.

11. Several smoothing time constants were used to obtain a measure of the kinetic content of different EMG patterns. For the present data, a time constant of 150 msec was used. A correction was made to the data on percentage of time active for the orbicularis oculi because the very short duration of the EMG bursts during eye blinks caused slight (10 percent) widening of the envelope, relative to the unsmoothed |EMG|. The computer sampling rate was 100 Hz in real time.
12. M. A. Johnson, J. Polgar, D. Weightman, D. Appleton, *J. Neurol. Sci.* **18**, 111 (1973).
13. For the large muscles for which superficial and deep biopsy data were reported, superficial data were selected for muscles from which recordings were made with surface electrodes.
14. D. C. King and K. M. Michels, *J. Exp. Psychol.* **53**, 113 (1957). Blink |EMG| duration was found to vary from 0.04 to 0.15 second. There were spontaneous tenfold variations in blink amplitude and rate in some individuals. A detailed account of the eye-blink data will be published (A. W. Monster, H. C. Chan, D. O'Connor, in preparation).
15. Similar type I percentages for the biceps brachii have been published elsewhere [M. H. Brooke and W. K. Engel, *Neurology* **19**, 221 (1965); Edström and Nyström (*3*)]. One possible explanation for the systematic deviation of the biceps brachii data in Fig. 2 is that a small percentage of superficial low-threshold motor units dominates the measurement of percentage of time active in this muscle. This explanation is supported by an analysis of the |EMG| amplitude distribution but contradicted by data on the usual intramuscular distribution of fiber types [item (i) in (*7*)].
16. The assumptions are that (i) fibers (or, rather, motor units) are consistently activated in the same way [E. Henneman, G. Somjen, D. O. Carpenter, *J. Neurophysiol.* **28**, 560 (1965); A. W. Monster and H. Chan, *ibid.* **40**, 1432 (1977)]; (ii) type I fibers are recruited before type II fibers; (iii) |EMG| amplitude is linearly related to the percentage of muscle fibers active [H. S. Milner-Brown and R. B. Stein, *J. Physiol. (London)* **246**, 549 (1975)]; and (iv) the |EMG| amplitude distribution, based on 8 hours of observation, is representative of the normal distribution of activity states of the muscle [item (ii) in (*7*)].
17. Intuitively, we expected T_A times to be correlated with the twitch contraction times of muscles; slowly (rapidly) contracting fibers need proportionally longer (shorter) T_A times to develop force. This intuitive bias is supported by a limited amount of human twitch contraction time data [F. Buchtal and H. Schmalbruch, *Acta Physiol. Scand.* **79**, 435 (1970); A. J. McComas and H. C. Thomas, *J. Neurol. Sci.* **7**, 301 (1968)]. The observed correlation between T_A time and percentage of type I fibers is thus in accordance with more fundamental findings [M. J. Barany, *J. Gen. Physiol.* **50**, 197 (1967)] relating fiber type to the speed of contraction of muscle fibers.
18. Supported by NIH grant NS 11574 NEUB and SRA grant 16-P-56804/5-08. We thank W. Freedman and J. P. Van Der Meulen for interest in the study and suggestions regarding the manuscript and K. Goodman for the audiovisual work.

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3-Methoxy-4-Hydroxyphenylglycol in Cerebrospinal Fluid and Vanillylmandelic Acid in Urine of Humans with Hypertension

Abstract. *3-Methoxy-4-hydroxyphenylglycol (MHPG) was measured in lumbar spinal fluid of 20 subjects with hypertension of varied etiology and severity. There was a significant correlation between the concentration of MHPG and the severity of hypertension. However, changes in the concentration of vanillylmandelic acid in the urine of these subjects were insignificant. In six subjects, administration of clonidine or α-methyldopa, two centrally acting antihypertensive drugs, was associated with a significant lowering of MHPG concentrations. These data support the hypothesis that central catecholamines are involved in clinical hypertension.*

The peripheral catecholamines do not seem to cross the blood-brain barrier (*1*). It appears that the brain catecholamine pool is distinct and unrelated to the peripheral biosynthesis of the amines. Catecholamines appear to have a neurotransmitter role in the brain (*2*). Noradrenaline (NA)-containing neurons (*3*), and more recently adrenaline-containing neurons (*4*), have been located in areas of the brain that are intimately concerned with cardiovascular control. Hence, a change in the activity of the catecholaminergic neurons may be reflected in disordered cardiovascular function.

Alterations of central catecholamine turnover, indicating altered rates of central release of the amines, have been observed in various types of experimental hypertension (*5*). Intraventricular injections of 6-hydroxydopamine, which selectively destroys central catecholaminergic neurons, prevented the development of experimental hypertension as well as spontaneous hypertension of rats (*6, 7*). The activity of tyrosine hydroxylase, the rate-limiting enzyme in the biosynthesis of catecholamines, was significantly reduced in the pontine locus coeruleus of patients with idiopathic orthostatic hypotension and Shy-Drager syndrome (*7, 8*).

Because there are few reports on the role of central catecholamines in human hypertension, we explored the possible involvement of brain catecholamines in clinical hypertension. To assess indirectly the rates of catecholamine turnover in the brain, we measured the concentration of 3-methoxy-4-hydroxyphenylglycol (MHPG), the major metabolite of brain NA and adrenaline in lumbar cerebrospinal fluid (CSF) according to a spectrophotofluorometric method of Korf *et al.* (*9*). To assess the peripheral catecholamine turnover, we estimated the amount of vanillylmandelic acid (VMA) excreted in the urine over 24-hour periods by means of the colorimetric method of Sunderman *et al.* (*10*).

Twenty patients with renal (*10*) and essential (*11*) hypertension of varying severity, and with blood pressures of 160/95 mm-Hg or above, were studied (13 males and seven females; age range 25 to 59 years, mean age 41.5 years). Eight patients with iron deficiency anemia (hemoglobin 9 to 11 g per 100 ml) recovering from ankylostomiasis were used as controls (five males and three females; age range 20 to 50 years, mean age 39.3 years). The blood pressures of the control subjects ranged from 120/75 to 130/85 mm-Hg, and they showed no evidence of any other disease. All the patients and the controls were of local Indian ancestry. All the patients with hypertension were subjected to detailed clinical and laboratory evaluation to determine the etiology and severity of their disease and its effects on the target organs.

Cerebrospinal fluid (10 to 15 ml) was obtained by lumbar puncture from all of the 28 subjects 7 to 15 days after they were admitted to the hospital. The CSF was stored at −20°C. The sample was discarded if blood was found in the CSF. The recoveries of the standard MHPG solutions were of the order of 70 to 80 percent. The amount of MHPG in the CSF was calculated by comparison with our standard recovery graph.

Six of the 20 patients with hypertension were chosen at random to be treated with clonidine or α-methyldopa so that we could study the effect of centrally acting antihypertensive drugs on the metabolites of central and peripheral

Table 1. Concentrations of MHPG in the CSF and urinary VMA excretion rates in control subjects and patients with hypertension. Urinary VMA was estimated in seven out of eight controls and 14 out of 19 patients with hypertension. One of the 20 patients with hypertension, in whom the disease was severe, had a very high concentration of MHPG (133 ng/ml) and was excluded from statistical analysis.

Group	MHPG (ng/ml)		VMA (mg/24 hours)	
	Number of subjects	Mean ± S.D.	Number of cases	Mean ± S.D.
Control	8	34.12 ± 11.32	7	4.08 ± 1.27
Hypertensive	19	53.00 ± 6.32*	14	4.89 ± 1.49†

*$P < .001$. †$P > .03$.

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