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Stefan Brutkowski, 1924—1966

OBITUARY

Stefan Brutkowski, 1924—1966

On October 28th 1966 Docent, Dr. Stefan Brutkowski was killed in a tragic street accident. He was member of the Department of Neurophysiology of the Nencki Institute of Experimental Biology, head of the Laboratory of Neuroanatomy in that Department and managing editor of Acta Biologiae Experimentalis. He was a member of the International Brain Research Organization, and of the Editorial Boards of two international journals: „Physiology and Behavior" and „Experimental Brain Research".

Dr. Brutkowski was born in Łódź on 13th February 1924. During the war, as a boy of 19, he was arrested by the Gestapo and sent to the concentration camp in Mauthausen where his elder brother was killed. After liberation, as an undergraduate student, he joined the Nencki Institute. He worked hard to overcome the inadequacies of his war time education and soon became a highly competent neurophysiologist. He obtained his doctor's degree in 1956 and became docent in 1960. From 1961 to 1965 he was head of the Department of Animal Physiology of Łódź University.

The first scientific study of Dr. Brutkowski was concerned with the effects of blood supply on mechanical and electrical excitability of peripheral nerves (see references 1, 4).

His subsequent work was devoted to the problems of higher nervous activity. The functional organization of the frontal agranular cortex was his main subject of research.

His experimental work was carried out on dogs, monkeys and rabbits in the Nencki Institute, in the National Institute of Mental Health U.S.A., and in the Physiological Department of the University of Łódź — respectively. The experimental procedure consisted in elaboration of salivary and/or motor conditioned reflexes, both excitatory and inhibitory, and in testing these reflexes after total or partial ablations of the frontal lobes. Excitatory reflexes were reinforced by presentation of food (in dogs and rabbits), introduction of acid into the mouth (dogs), or electric stimulation of the leg (dogs). It has been shown that frontal lesions produce a number of changes in animal behaviour, among which the increase of reactivity, increase of the conditioned reflex activity in the intertrial intervals, and disinhibition of inhibitory conditioned reflexes to negative stimuli are the most prominent. In some cases the primitive responses established in earlier periods of life and thereafter suppressed by more specialized reactions tend to appear. In experiments with alimentary conditioned reflexes, the animals display an increase of hunger drive, manifested by the strong tendency to reach food, to lick the empty food-bowl and so on. This „drive disinhibition" is not necessarily connected with the increase of food intake.

Recent experiments performed on dogs and rabbits have shown that drive disinhibition is produced by lesions of medial parts of the frontal area, whereas in monkeys it is produced by orbito-frontal lesions.

The results of these studies were published in papers: 2, 3, 5—7, 9—12, 14—18, 20, 21, 26—29, 31—33, 35—45 of the reference list, below.

Stefan Brutkowski's further work was concerned with some structures anatomically and functionally related to the frontal cortex. It was shown that the syndrome of drive disinhibition could be obtained after partial lesions of hypothalamus (rabbits), amygdala (dogs), dorso-medial thalamic nucleus (dogs) and area genualis (dogs) (items: 19, 22—25, 29, 32, 34, 36—38, 40, 41, 43, 47).

Recently he undertook neuroanatomical studies on dogs, aiming at the elucidation of connections between frontal lobes and diencephalon, in particular with dorso-medial thalamic nucleus (46).

Stefan Brutkowski portrayed the highest qualities of character in his high moral standards, sense of honour, duty and comradeship. He possessed great enthusiasm for scientific work, and to his younger colleagues he freely gave of his time and advice. He was undoubtedly a model for the young generation of scientific workers whom he trained both in the Nencki Institute and in the Łódź University.

It is no wonder that he was a very popular figure among neurophysiologists and psychologists and had a wide circle of sincere friends not only in Poland but also in other countrie. His death is a loss to neurophysiology and will be greatly missed.

J. Konorski

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ETUDE EEG CHEZ L'ANIMAL ET CHEZ L'HOMME D'UN MODE D'ASSOCIATION SPECIFIQUE, DISTINCT DU CONDITIONNEMENT CLASSIQUE, L'ACQUISITION LIBRE

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(*Reçu le 25 Avril 1966*)

Il est généralement admis que les principales acquisitions de l'enfance et de l'âge adulte sont le résultat d'associations qui relient certains faits à leurs conséquences. Cette aptitude à établir un lien entre des événements qui se succèdent est utilisée aussi bien dans les apprentissages scolaires que dans le dressage. Les mots à prononcer ou les gestes à effectuer sont suivis d'une récompense, les mots et gestes à éviter suivis d'une punition.

L'une des formes les mieux étudiées de ces acquisitions est sans conteste le réflexe conditionné qui, pour apparaître, nécessite l'application de stimulations sous forme de couples. Pour Pavlov (1929) en effet deux conditions fondamentales sont nécessaires à la formation de ce réflexe: d'une part, la combinaison des deux stimulations dans le temps, d'autre part, le décalage du stimulus conditionnel qui précéde le stimulus inconditionnel.

Pourtant il ne semble pas que ce réflexe conditionné puisse recouvrir l'ensemble des acquisitions car certaines d'entre elles se développent en dehors de cet ordre chronologique rigoureux entre les stimulations. C'est ce qu'on observe chez l'animal dans les activités de jeu. C'est également ce que signalent chez l'homme, certains auteurs attentifs aux phénomènes psychologiques. Proust („Du coté de chez Swann") par exemple, mentionne qu'au moment où un morceau de gâteau s'émiette dans sa bouche, surgit brusquement dans sa mémoire l'apparition de sa tante effectuant les ges-

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[1] Chargé de recherches au CNRS.

tes qui précédaient immédiatement l'offre du gâteau et son ingestion. Dans cet exemple, le stimulus inconditionnel, l'alimentation, semble déclancher l'apparition des impressions conditionnées.

En Psychologie et en Physiologie différents travaux ont signalé l'existence d'acquisitions survenant indépendamment de tout ordre chronologique entre les stimulations. Un tel phénomène est fréquemment observé dans des expériences effectuées par des auteurs Anglo-Saxons (Bernstein 1934, Grether 1938, Harris 1941, Wickens et Wickens 1942) qui ont mis en évidence des réflexes acquis sans que les stimuli soient combinés. Ces réflexes sont provoqués par le stimulus neutre A, aprés l'application d'une ou plusieurs séries de stimuli B ou encore aprés la distribution sous une forme dispersée de A et B à des intervalles de temps variables et sans ordre particulier. Les réflexes ainsi obtenus seraient moins spécifiques que les réflexes conditionnés, et sont dits pseudoconditionnés. C'est ainsi que Bernstein (1934) utilisant comme stimulus inconditionnel une stimulation électrique appliquée sur la région orbitaire de l'homme et provoquant un réflexe palpébral, montre qu'en appliquant au hasard, tantôt des séries de sons, tantôt des séries de stimulations orbitaires, on observe l'apparition de mouvements palpébraux provoqués par le son.

A la même époque deux réflexologistes Russes, Narbutovitch et Podkopayev (1936) appliquant des stimuli capables de provoquer des réactions d'orientation (son, lumière, rotation d'un objet...) observent qu'après un certain nombre d'essais, l'application de l'un de ces stimuli détermine une réaction d'orientation dirigée vers la source de l'autre.

Des expériences d'inspiration différente et poursuivies en France, en Allemagne et en Russie, aboutissent à des résultats analogues qui ont été rapportés dans un ouvrage récent (John 1962). Leur origine est relativement ancienne et remonte à Brown-Sequard qui en 1884, stimule d'abord l'aire visuelle du cortex du chien sans observer de réponse, puis stimulant simultanément l'aire visuelle et l'aire motrice, obtient un mouvement, enfin stimule à nouveau l'aire visuelle seule et provoque le mouvement. Or, cette expérience ne comporte pas de décalage entre la stimulation occipitale „conditionnée" et la stimulation centrale „inconditionnée". Quelques années plus tard Baer (1905) réalise des expériences du même type sur des chiens porteurs d'électrodes à demeure. A la même époque Wedenski (1935) puis Uchtomski (1950), puis plus tard Popov (1950) introduisent la notion de Dominanta qu'on peut définir de la façon suivante: si un récepteur ou une règion du cerveau donnant un rèflexe déterminé est stimulé pendant une durèe suffisante, des modifications inapparentes surviennent et se traduisent par le fait gu'une autre stimulation, appliquée sur n'importe quel récepteur, provoquera le même réflexe bien qu'à aucun moment les deux stimulation n'aient été couplées.

C'est ainsi que dans une expérience de dominance, Popov (1950) stimule pendant dix jours la patte d'un pigeon à l'aide d'un courant induit. Il constate ensuite que des stimulations auditives faibles, primitivement neutres, provoquent un retrait violent de la patte de l'animal.

Dans ces expériences de dominance, comme dans les expériences de pseudoconditionnement, une réponse acquise apparaît sans que les stimulations aient été couplées. Cependant une certaine opposition semble se manifester entre les expériences de pseudoconditionnement qui utilisent des stimuli faibles et les expériences de dominance qui nécessitent des stimuli forts. En fait, cette opposition est levée par l'électrophysiologie qui, mettant en èvidence des réponses subliminaires, a permis d'observer des phénomènes de dominance avec des stimulations d'intensité relativement faible (Rusinov 1953, Novikova et Farber 1956, Sokolowa 1958, Lelord et Popov 1960).

Quoiqu'il en soit les relations pouvant exister entre les réflexes pseudoconditionnés et de dominance d'une part, les réflexes conditionnés d'autre part, restent à préciser. Pour certains auteurs, seul le réflexe conditionné est spécifique, les autres réflexes constituent des phénomènes de réactivation ou de facilitation pouvant être provoqués par n'importe quelle stimulation. Ils s'apparentent à la réaction de sursaut ou à des réactions de défense peu élaborées. D'autres auteurs, au contraire, estiment qu'une certaine parenté unit tous ces phénomènes. C'est ainsi que pour Grether (1938) le mécanisme du pseudoconditionnement „se retrouve dans le conditionnement et notamment le conditionnement de type émotionnel".

Etant donné l'importance théorique d'un tel problème, nous nous sommes attaché à préciser les caractéres de ces différents types de réactions.

Pour effectuer une telle étude une méthode de conditionnement classique pouvait être utilisée, qu'il s'agisse de la méthode salivaire de Pavlov (1929) ou de la méthode motrice ou salivomotrice de Konorski (1930). De fait, certaines expériences préliminaires effectuées dans le laboratoire de Konorski autorisaient à utiliser le mouvement du chien pour analyser des modes d'acquisition différents (Konorski communication personnelle).

Nous avons cependant préféré avoir recours aux méthodes électrophysiologiques. En effet, depuis l'observation initiale de Durup et Fessard (1935), de nombreux auteurs ont montré que les réponses électrophysiologiques, tout comme les réflexes périphériques et les mouvements, pouvaient être conditionnées. Bien plus, l'étude parallèle des réflexes périphériques et de ces réponses montre qu'elles apparaissent de façon plus précoce et permettent de déceler des phénomènes subliminaires. La méthode électrophysiologique permet en outre d'utiliser le conditionnement pour étudier des stimulations sensorielles, stimulations qui du fait de leur innocuité peuvent être appliquées chez l' homme comme chez l'animal. Enfin des expériences relativement récentes montrent que l'électrophysiologie convient particulièrement à l'étude des acquisitions obtenues à l'aide de stimulations dispersées. Varga et Pressman (1961) enregistrent l'électromyogramme chez l'animal et distribuent sans aucun ordre particulier tantôt un son, tantôt une stimulation somatique faible (flexion passive d'un membre). Ils observent qu'après quelques essais, le son provoque une réponse électromyographique au niveau du membre intéressé. Popov (1958) utilise l'électroencèphalogramme chez l'homme et montre qu'après l'intervention de trois stimulations lumineuses appliquées successivement, le son primitivement neutre provoque une réponse EEG prolongée dont l'aspect n'est habituellement observé qu'après la stimulation lumineuse. C'est cette stimulation que nous avons utilisée dans l'étude présenté.

TECHNIQUE

Dans les expériences effectuées ici le stimulus inconditionnel est constitué par deux éclairements successifs de 250 ms séparés par un intervalle de 500 ms ce qui constitue une stimulation totale d'une seconde. La source lumineuse est une lampe à réflecteur alimentée par le secteur: placée à un mètre du visage de l'homme une lampe de 100 watts donne un éclairement de 650 lux, fixée à 80 cm de l'oeil du lapin une lampe de 250 watts donne un éclairement de 3200 lux.

Le stimulus conditionnel est un son continu d'une durée de 4 secondes. Chez l'homme son intensité est de 36 décibels au dessus du seuil d'audibilité, sa fréquence de 1100 c/s. Le son à dofférencier est d'intensité sensiblement égale (42 décibels) et plus grave (800 c/s). Chez le lapin l'intensité du stimulus conditionnel est faible, de 1 décibel au dessus du seuil et sa fréquence élevée (2 000 c/s). Le son à différencier est grave (700 c/s) et son intensité de 7 décibels au dessus du seuil. Que l'expérience soit effectuée chez l'animal ou chez l'homme, le sujet est placé dans une pièce où l'obscurité est totale et où les conditions de silence sont satisfaisantes. L'homme est assis dans un fauteuil confortable; il porte un casque léger sans mentonnière permettant de maintenir l'adhérence des électrodes au cuir chevelu; les dérivations bipolaires sont vertico-temporales droite et gauche, temporo-occipitales droite et gauche. Le lapin est immobilisé sur un cadre de contention qu'il tolère facilement après 2 ou 3 séances d'adaptation; la tête de l'animal est fixée dans un étau peu serré; les électrodes posées sous anesthésie sont fixées à demeure suivant le procédé de Libouban et Aleonard (1960); les dérivations monopolaires réunissent une électrode placée dans le sinus frontal aux électrodes pariétales et occipitales droites, pariétales et occipitales gauches.

L'appareil d'enregistrement est un électroencéphalographe à 6 canaux de type courant.

Tracé et réponses EEG. Chez l'homme la réponse étudiée est la disparition du rythme alpha ou réaction d'arrêt provoquée par la stimulation et dont on mesure la durée. Chez le lapin nous appellerons par analogie „réaction d'arrêt" la disparition du rythme alpha ou réaction d'arrêt provoquée par la simulation et dont on mesure à 8 c/s qui s'apparente aux activités thêta.

La première fois que le son est appliqué, il peut provoquer une réaction d'arrêt pendant quelques secondes, mais au fur et à mesure que cette stimulation est répétée, la réponse qu'elle provoque diminue et disparaît généralement à la 4ème ou 5ème répétition (fig. 1).

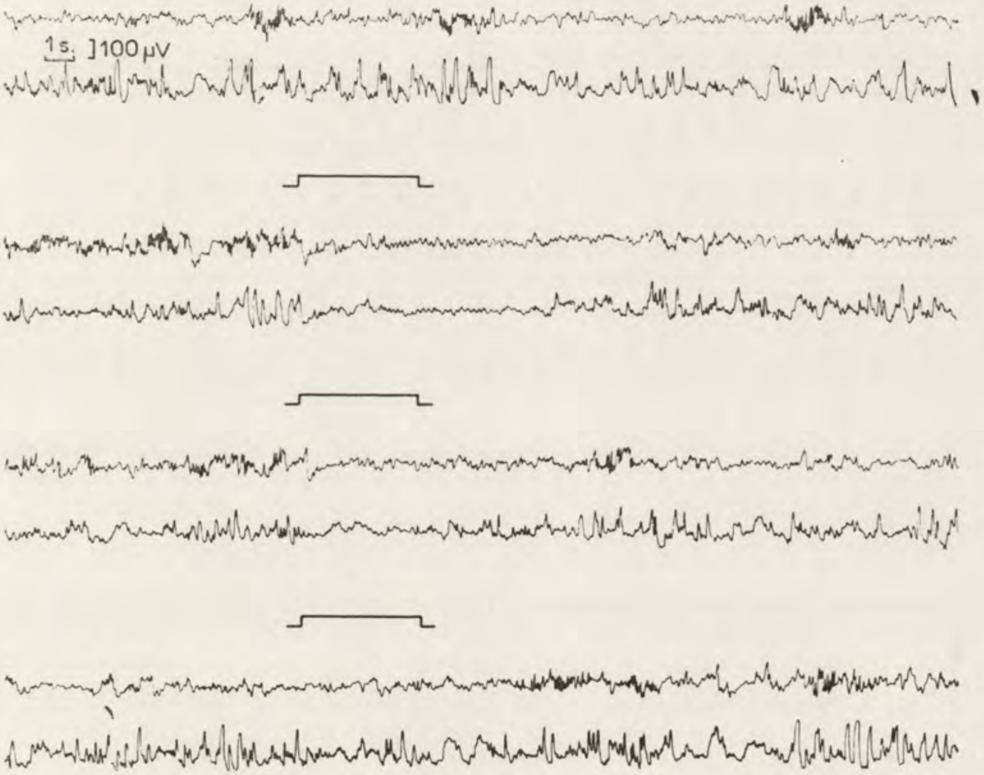


Fig. 1. Tracé EEG de lapin. Ligne supérieure: dérivation pariétale, ligne inférieure: dérivation occipitale. De haut en bas: tracé spontané, réactions d'arrêt au Ier, 3ème et 5ème son. Chaque son est représenté par un plateau. On voit que la répétition du son entraine la disparition de la réponse.

La stimulation lumineuse donne par contre un effet plus marqué et plus stable (fig. 2). Répétée à des intervalles de temps suffisants, elle provoque de façon très régulière sur le traçé une réaction d'arrêt dont la durée varie suivant les sujets de

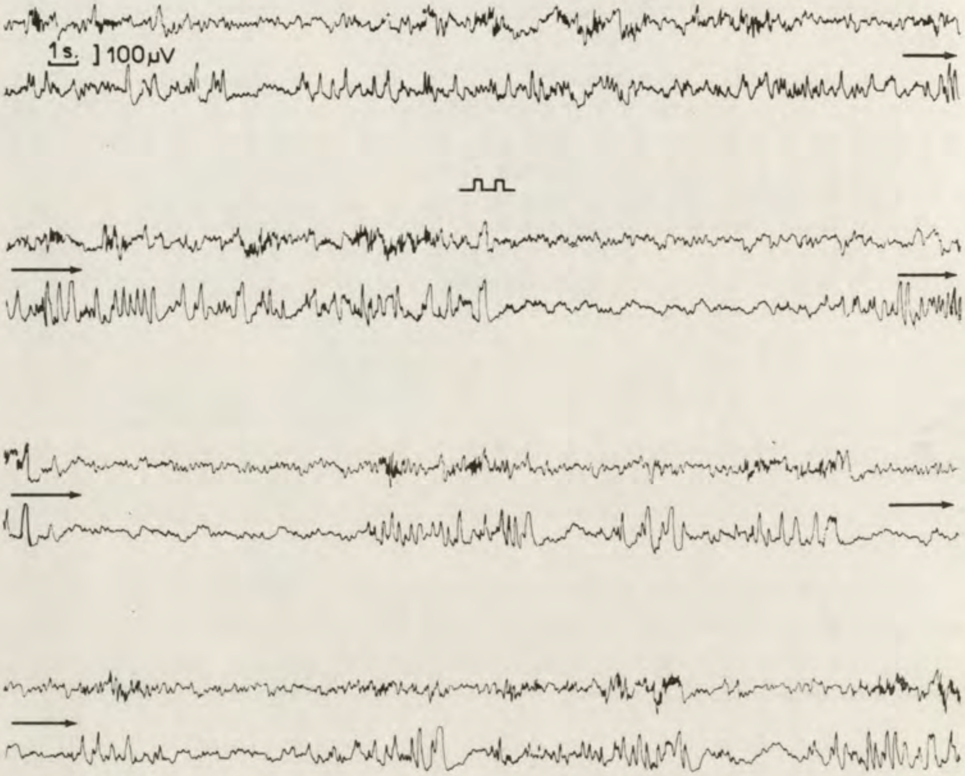


Fig. 2. Tracé EEG de lapin. Ligne supérieure: dérivation pariétale, ligne inférieure: dérivation occipitale. De haut en bas = tracé spontané, réaction d'arrêt et action prolongée provoquée par la stimulation lumineuse (créneaux). La réaction d'arrêt dure 12 secondes, l'action prolongée persiste environ 30 secondes.

quelques secondes à plus d'une minute. Cette réponse peut être conditionnée et apparaître de façon régulière après le son seul (fig. 3).

Afin de permettre l'objectivation des réactions d'arrêt, les stimulations ne sont appliquées que lorsque le tracé EEG présente un aspect bien déterminé: rythme alpha chez l'homme, oscillations variant de 3 à 7 cycles par seconde et de 100 à 300 microvolts chez le lapin. En effet, la durée de la réaction d'arrêt varie avec l'aspect du tracé spontané. Elle augmente lorsque l'amplitude du tracé est réduite et que rythme de base n'apparaît plus que par brèves bouffées. Elle diminue lorsque le tracé est ample et présente de nombreux rythmes lents. C'est pourquoi chez l'homme les expériences ne portent que sur des sujets présentant un rythme alpha apparent et aucune stimulation n'est appliquée avant que les réactions d'arrêt consécutives à la stimulation précédente n'aient complétement disparu. Il en est de même chez le lapin qui pose en outre des problèmes particuliers liés aux variations importantes de son tracé EEG pouvant aller de l'aspect plat aux oscillations amples de 250 à 400 microvolts et de fréquence lente de 2 à 5 c/s.

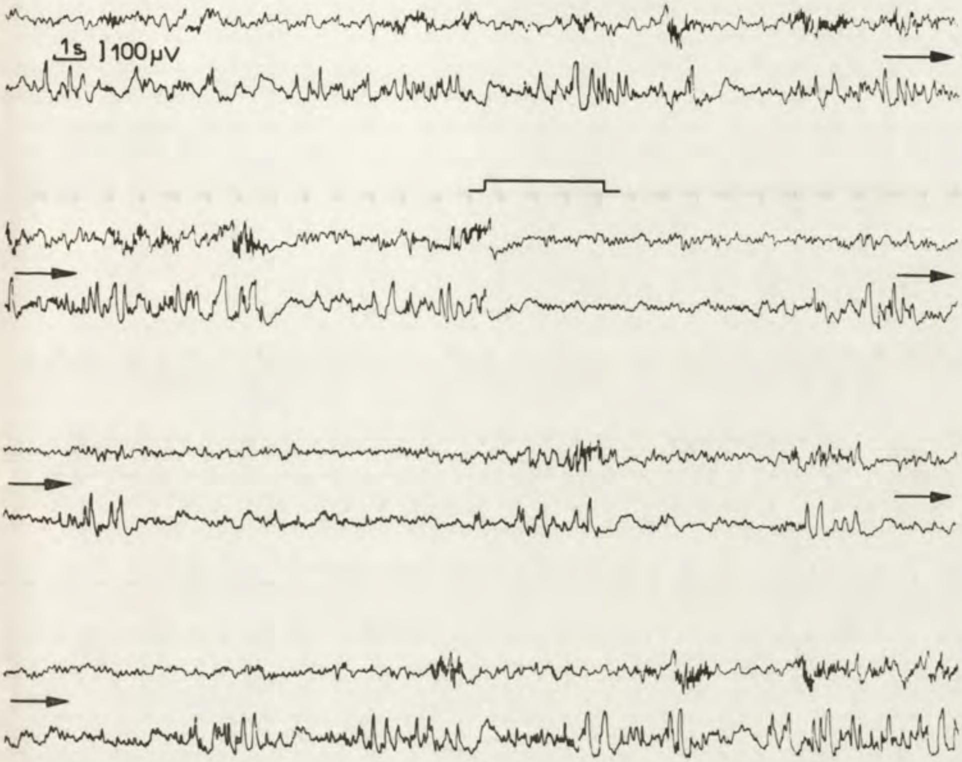


Fig. 3. Tracé EEG de lapin. Ligne supérieure: dérivation pariétale, ligne inférieure: dérivation occipitale. De haut en bas: tracé spontané, réaction d'arrêt et action prolongée provoquée par le son çonditionné (plateau). La réaction d'arrêt dure 10 secondes, l'action prolongée persiste pendant prés d'une minute.

Ces aspects extrêmes ne permettent pas de suivre le conditionnement de la réaction d'arrêt, nulle lorsque le tracé est ample et non mesurable lorsque le tracé est plat. Ils amènent à interrompre les stimulations et nécessitent soit une attente de plusieurs minutes, soit une intervention de l'expérimentateur pour „rassurer" ou „réveiller" l'animal, voire même une interruption complète de l'expérience.

Protocole experimental. Les précautions habituelles au conditionnement Pavlovien ont été respectées dans les expériences d'électrophysiologie. Le rythme des séances est de trois par semaine, chaque séance n'excédant pas une heure et comportant l'application de 8 à 16 stimulations données à des intervalles de temps qui varient habituellement entre 40 secondes et trois minutes et demie (les interruptions plus longues n'étant pas comprises içi).

Dans les expériences de conditionnement „classique", le stimulus inconditionnel est toujours donné dans des couples de stimulations combinées où le son précède pendant une seconde et demie, accompagne pendant une seconde et suit pendant une seconde et demie la stimulation lumineuse qu'il „chevanche" (fig. 4, Protocole 2).

Dans les expériences de stimulations dispersées le stimulus inconditionnel est toujours séparé du stimulus inconditionnel. Il n'y a plus de combinaison mais simplement une succession de stimulations isolées, chronologiquement indépendantes. Dans ces deux types d' expériences le nombre de sons seuls est supérieur au nombre généralement mentionné dans les expériences de conditionnement classique. Cela tient au fait que la réaction d'arrêt conditionnée est moins sujette à l'extinction que le réflexe conditionné, et qu'il est possible d'appliquer souvent le son seul sans compromettre le conditionnement. Aussi chaque séance comporte-t-elle à peu près autant de stimulations conditionnées données seules que de stimulations inconditionnées (lumière dans les expériences de stimulations dispersées, combinaisons son-lumière dans les expériences de conditionnement).

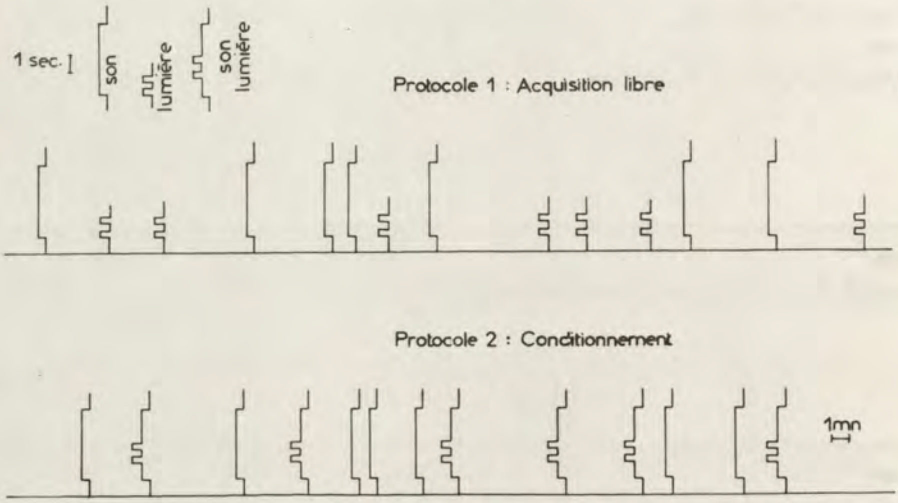


Fig. 4. Méthodes de distribution des stimulations. Eu haut stimulations dispersées: la lumière est appliquée seule et séparée du son par des intervalles de temps variables. En bas, stimulations combinées: la lumière est toujours combinée avec le son. Plateau: son, créneaux: lumière.

Dans tous les cas les stimulations qu'elles soient isolées ou couplées se succédent comme dans le conditionnement classique, c'est-à-dire sans ordre particulier, sans séquence stéréotypée, comme l'indique la fig. 4: soit S le son, L la lumière seule, C la combinaison son-lumière, on voit que la séance de stimulations dispersées est constituée par les suites S LL SSS L S LLL SS L et que la séance de conditionnement comporte les suites S C S C SSS CCC SS C. Le programme de ces suites des expériences de conditionnement est parfois préétabli par certains auteurs qui se réfèrent aux tables de hasard. Cela n'était pas possible içi car toutes les fois que l'aspect du tracé s'écartait de l'aspect pris comme référence, sans pour cela devenir tout à fait plat ou au contraire très ample avec des ondes lentes, c'est un stimulus inconditionnel (lumière seule, ou combinaison son-lumière suivant le type de séance) qui était appliqué. L'expérience montre en effet que ce stimulus est souvent capable à lui seul d'entraîner à la fin de la réponse qu'il provoque, le rétablissement de l'aspect du tracé de base. Ce procédé se justifiait également par le fait que la durée de la réaction d'arrêt inconditionnée nécessairement modifiée par la présence de ces aspects atypiques du tracé, n'intervenait pas dans nos calculs.

Il en résultait que le contrôle de la distribution des stimulations était effectué non pas avant mais après chaque séance et toutes les trois ou quatre séances. L'emploi de tables de hasard restait possible en suivant une méthode inspirée de Swed, Frieda et Eisenhart (comp. Siegel 1956) et nous a permis de nous assurer que notre distribution ne différait pas de façon significative d'une distribution au hasard.

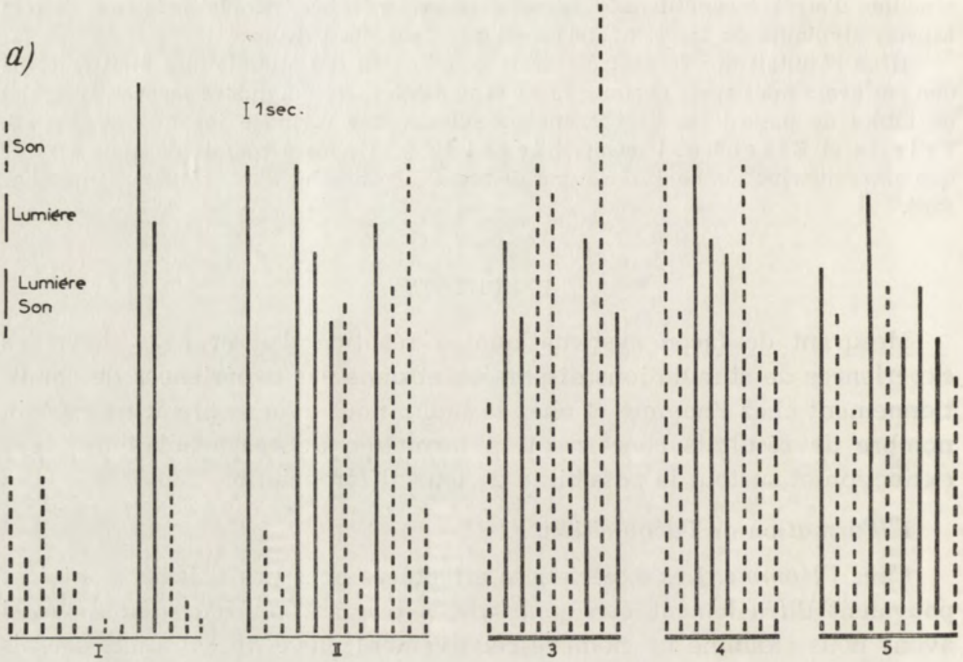
RESULTATS

Mesurant de façon systématique la réaction d'arrêt EEG dans des expériences de stimulations dispersées et dans des expériences de conditionnement chez l'homme et chez le lapin, nous avons obtenu un certain nombre de résultats concernant la formation de ces acquisitions, leur extinction et surtout la possibilité de leur différenciation.

1°/*Formation de l'acquisition.*

Chez l'Homme. Les expériences effectuées chez des sujets volontaires pouvaient difficilement être poursuivies pendant plusieurs mois. Aussi avons nous examiné un nombre relativement élevé de 56 sujets soumis à des séries de 5 à 6 séances, 2 à 3 séances de stimulations dispersées pendant une semaine suivies d'une interruption de quinze jours à un mois et d'une reprise de 3 séances de stimulations combinées pendant une semaine. Le fait le plus frappant de cette étude est que les variations individuelles si marquées dans le conditionnement au son et à la lumière chez l'homme (Lelord et al. 1960), se retrouvent de la même façon au cours des séances de stimulations dispersées.

Nous en donnerons pour exemple deux profils résumant les expériences effectuèes chez deux sujets très différents (fig. 5). Les séances I et II correspondent aux expériences de stimulations dispersées et les séances 3, 4 et 5 aux expériences de conditionnement. Il est frappant de constater que le conditionnement, très apparent chez le sujet Za (en haut) puisque les réponses conditionnées atteignent une durée égale aux réponses inconditionnèes (3, 4, 5), semble déjà se manifester au cours des séances de stimulations dispersées (I, II). Au contraire et de la même façon le conditionnement non apparent chez Bo (en bas) est précédé de modifications minimes au cours des séances de stimulations dispersées. La comparaison par la méthode du U de Mann et Whitney des durées des réactions d'arrêt mesurées au cours de toutes les séances de stimulations dispersées ($m = 6,3$ s) aux durées de toutes les réactions d'arrêt conditionnées ($m = 8,3$ s) pour les 56 sujets montre que les chiffres obtenus sont peu différents ($p > 20$). Il semble donc que l'acquisition par le son d'une propriété qui rend a)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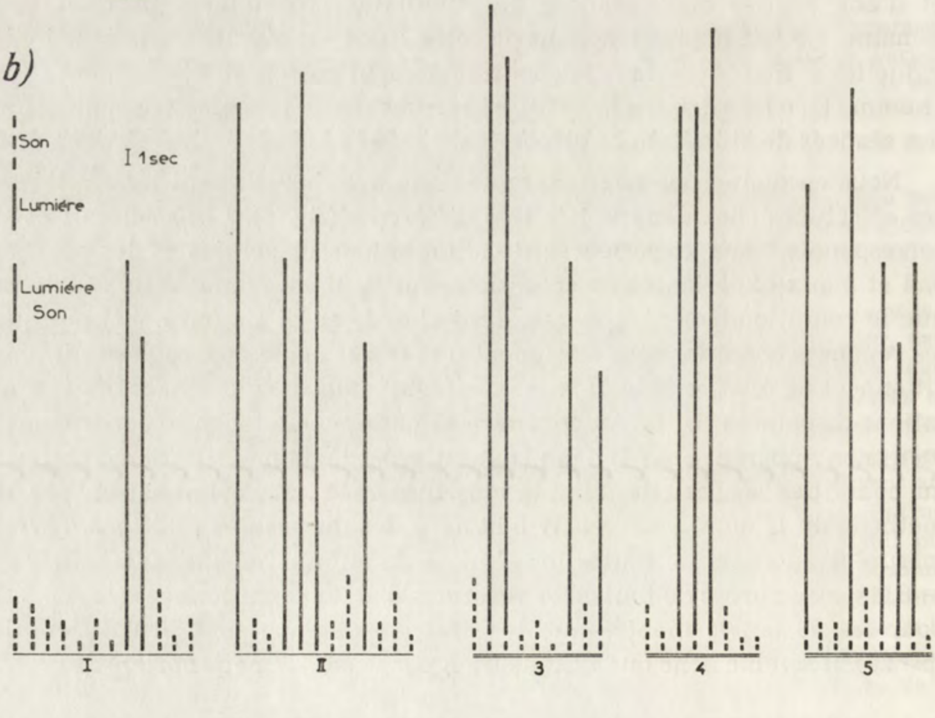
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cette stimulation capable de provoquer des réactions d'arrêt marquées et stables se manifeste chez l'Homme quel que soit le mode de distribution des stimulations (Lelord et Charue 1960).

Chez le lapin. Les expériences ont pu être poursuivies pendant des périodes de plusieurs mois. Etant donnée la variabilité des réponses observées chez cet animal, les sujets ont été choisis avec soin. Ce sont 4 ,,Géants des Flandres" âgés de 18 mois à 3 ans présentant un rythme de base stable et des réponses régulières à la stimulation lumineuse. De 8 à 13 séances de stimulations dispersées sont effectuées et suivies, après un intervalle de un à deux mois, de 8 à 17 expériences de conditionnement.

La figure 6 montre les 3ème, 5ème et 8ème expériences effectuées au cours d'une première série d'expériences de stimulations dispersées et d'une deuxième série d'expériences de stimulations combinées chez le lapin ,,Placide".

En haut, le profil 3 qui correspond à la troisième séance d'extinction du son, traduit l'absence presque totale de réponse. Au milieu le profil correspond à la deuxième séance de stimulations dispersées et montre au contraire l'apparition après le son (tirets) de réactions d'arrêt de 3 à 4 secondes. Ces réponses persistent sur le profil 8 qui correspond à la cinquième séance de stimulations dispersées.

Des résultats presque identiques sont observés en bas de la figure au cours des séances de conditionnement: absence de réponse pendant l'extinction du son (profil 3), augmentation de la réaction d'arrêt au son au cours des 2ème et 5ème séance de conditionnement (profils 5 et 8).

La comparaison par la méthode du U de Mann et Whitney des durées des réactions d'arrêt mesurées chez les lapins Placide, Persan, Picaro et Orphée successivement dans les séances de stimulations dispersées (m = 5,9 s) et dans les séances de conditionnement (m = 6,2 s) montre que les résultats obtenus sont peu différents ($p > 0.20$).

Ces séries expérimentales de longue durée poursuivies chez quatre lapins confirment donc les résultats des séries expérimentales brèves effec-

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Fig. 5. Expériences d'acquisition chez le sujets Za et Bo; En abscisses = Les stimulations groupées par séances: I et II stimulations dispersées, 3, 4, et 5 stimulations combinées. En ordonnées = La durée des réactions d'arrêt au son (tirets), à la lumière seule (traits pleins), aux combinaisons son-lumière (traits pleins marqués de tirets).

En haut, augmentation rapide de la réponse au son aprés l'intervention de la lumière (II), qui s'accentue avec les combinaisons (3, 4, 5) chez le sujet Za.

En bas, absence de modification des réactions d'arrêt au son que la lumière soit dispersée (II) ou combinée (3, 4, 5) chez le sujet Bo.

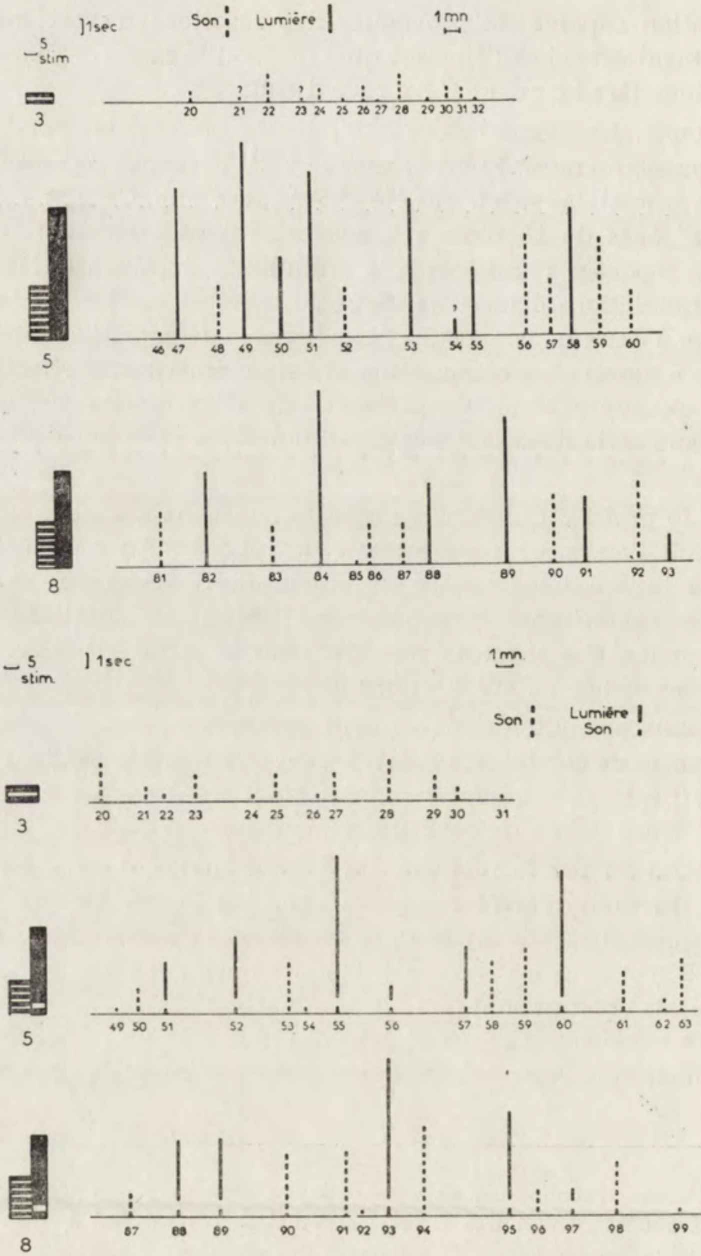

Fig. 6. Expériences d'acquisition chez le lapin. En abscisses: les stimulations de l'expérience séparées par des intervalles de temps différents. En ordonnées: la durée des réactions d'arrêt au son (tirets), à la lumière (traits pleins) aux combinaisons son-lumière (traits pleins marqués d'un tiret). A gauche, représentation schématique par suppression des intervalles de temps et de l'ordre des stimulations. L'épaisseur des colonnes correspond au nombre des stimulations, la hauteur à la durée moyenne des

tuées chez l'homme. Elles montrent que la réaction d'arrêt acquise a sensiblement la même durée, que les stimulations soient combinées ou qu'elles soient dispersées.

2°/*Extinction de l'acquisition.*

Ce phénomène décrit au cours du conditionnement est ici évident et ne mérite qu'une étude brève. Les réponses acquises par la méthode dispersée diminuent comme les réponses conditionnées lorsqu'on répète le son seul. C'est ce que montre le schéma de la figure 7 où la comparaison des deux séries de colonnes met en évidence un fait très général: l'extinction du son est plus rapide après les expériences de stimulations dispersées qu'après le conditionnement.

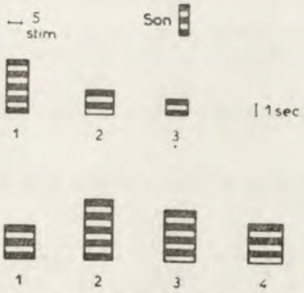

Fig. 7. Expériences d'extinction du son. Chaque colonne à bande noire résume une expérience d'extinction du son, l'épaisseur de la colonne est proportionnelle au nombre de stimulations, sa hauteur, à la durée moyenne des réponses. En haut, 3 expériences d'extinction du son après une série d'expériences de stimulations dispersées. En bas, 4 expériences d'extinction du son après une série d'expériences de conditionnement.

3°/*Différenciation de l'acquisition.*

Les résultats précédents semblent montrer que ni la formation de l'acquisition, ni son extinction ne paraissent très influencées par le mode de distribution des stimulations. C'est dire l'importance cruciale des expériences de différenciation.

En effet, le caractère spécialisé, électif, du réflexe conditionné fait partie de sa définition même. Une fois la différenciation établie, le sti-

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réponses, au son (colonne à bandes noires et blanche), à la lumière (colonne noire), aux combinaisons son lumière (colonne noire à base blanche). En haut, la lumière est donnée seule dans les expériences de stimulations dispersées. En bas, la lumière est combinée au son dans les expériences de conditionnement.

mulus conditionné doit provoquer le réflexe alors qu'un stimulus voisin reste sans effet. C'est ce que montre la figure 8. En haut le tracé est modifié par le son conditionné. En bas le son différencié reste sans effet.

On peut alors se demander si les couples de stimulations ne sont pas nécessaires à la réalisation de la différenciation car l'adjonction d'un son

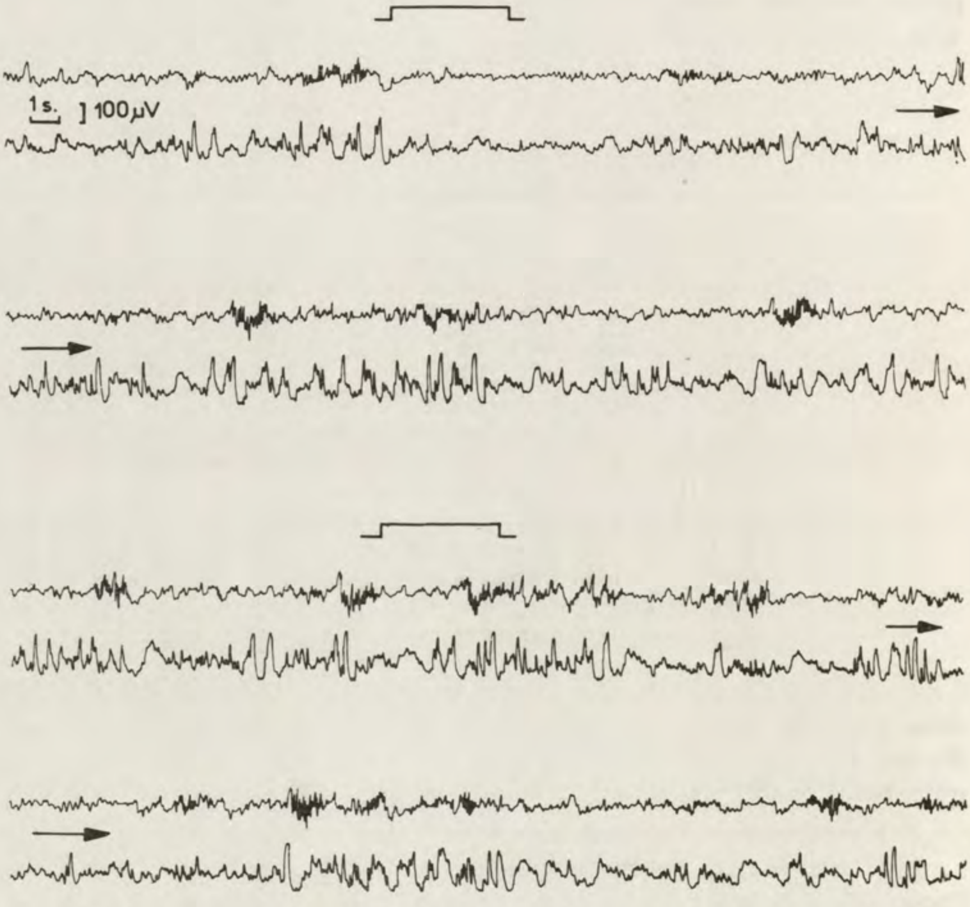


Fig. 8. Traces EEG de differenciation chez le lapin. Ligne supérieure: dérivation pariétale, ligne inférieure: dérivation occipitale. En haut: le réaction d'arrêt au son aigu conditionné dure huit secondes. En bas: la réaction d'arrêt au son grave différencié dure une seconde et demie (les plateaux indiquent les durées des sons).

différent dans une expérience de stimulations dispersées ne peut prêter qu'à confusion. C'est pourquoi il est nécessaire dans ce type d'expérience, de recourir à un protocole particulier (fig. 9). Des séances de stimulations dispersées du son aigu (SA) et de la lumière (L) sont suivies d'autres séances où le son grave (SG) est donné seul (Acquisition libre-séances I). Après avoir effectué un certain nombre de ces expériences, on introduit dans une séance de stimulations dispersées un ou deux sons graves et dans une séance de sons graves un ou deux sons aigus (Acquisition libre-séances II).

Ce protocole peut être comparé à la différenciation du conditionnement classique schématisé en haut de la figure.

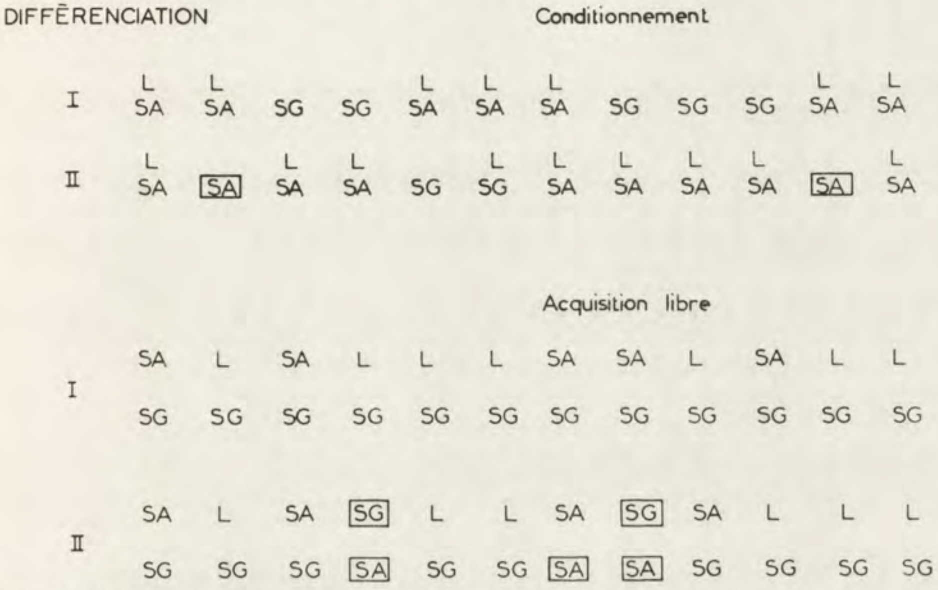


Fig. 9. Méthodes de différenciation. S.A. = Son aigu, S.G. = son grave, L = Lumière. Conditionnement. Séance I: succession de sons aigus combinés avec la lumière et de sons graves seuls. Séance II: de temps à autre un son aigu est donné seul pour permettre une comparaison des réponses au son aigu et au son grave. *Acquisition libre.* Séances I: distribution sous une forme dispersée du son aigu et de la lumière, ou de sons graves donnés seuls. Séances II: sons graves introduits dans une séance de stimulations dispersées, ou sons aigus introduits dans une séance de sons graves.

Chez le lapin. Nous donnerons pour mémoire le schéma d'une séance de différenciation par la méthode classique chez le lapin Niger (fig. 10, profil 24). On voit que les réponses au son aigu (tirets) sont 3 à 4 fois plus élevées que les réponses au son grave. Au cours d'une autre séance (fig. 10, profil 29) où ne sont appliqués que des sons aigus et des sons graves, la même différence apparaît entre les durées des réponses.

La figure suivante représente le résultat de 31 séances de différenciation chez ce lapin (fig. 9). Cette différenciation est établie à partir de la séance 24 puisque les réponses au son aigu sont alors 3 fois plus élevées que les réponses au son grave.

Ce sont des séries d'expériences du même type, mais utilisant cette fois le protocole des stimulations dispersées (fig. 9, acquisition libre) qui ont été effectuées chez trois lapins. Chez deux d'entre eux une différenciation nette entre les sons aigu et grave a été observée. C'est ce que montre

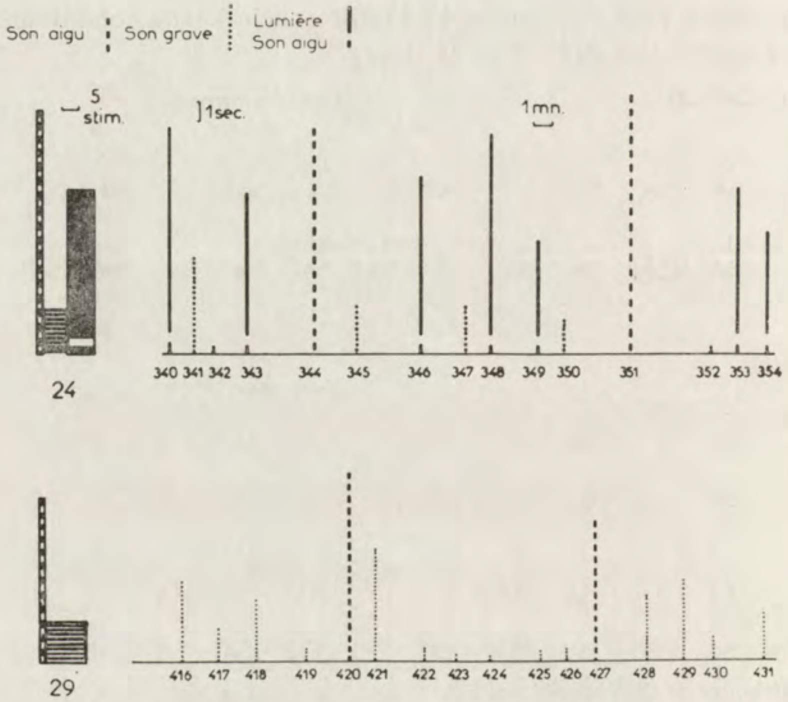


Fig. 10. Expérience de différenciation conditionnée chez le lapin. En abscisses = les stimulations de l'expérience séparées par des intervalles de temps différents. En ordonnées = la durée des réactions d'arrêt au son aigü (tirets) au son grave (pointillés aux combinaisons du son aigu et de la lumière (traits pleins marqués d'un tiret). A gauche représentation schematique par suppression des intervalles de temps et de l'ordre des stimulations. L'épaisseur des colonnes correspond au nombre des stimulations, la hauteur à la durée moyenne des réponses au son aigu (colonne à bandes noires et blanches), au son grave (colonne à hachures), aux combinaisons son-lumière (colonne noire à base blanche).

le schéma de la figure 12 qui résume les 43 séances effectuées chez le lapin Niger avant la série de conditionnement différencié prise comme exemple précédemment. On note cependant qu'avec cette méthode dispersée, la différenciation n'est pas stable et qu'elle disparaît à partir de la séance 32. Au cours des expériences suivantes, les réponses au son aigu

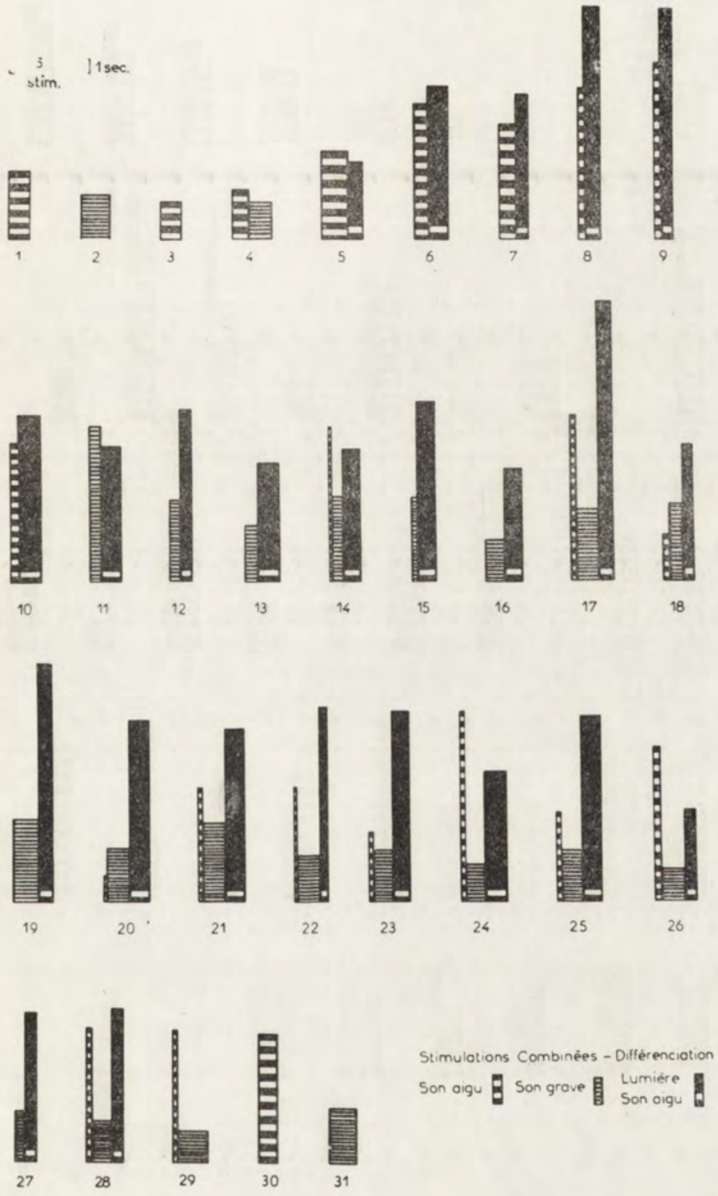


Fig. 11. Série de 31 expériences de differenciation conditionnée chez le lapin. Colonnes à bandes noires et blanches: son aigu, colonnes à hachures: son grave, colonnes noires à base blanche: combinaisons du son aigu et de la lumière. L'épaisseur des colonnes correspond au nombre des stimulations, la hauteur à la moyenne des durées des réactions d'arrêt correspondantes. De 1 à 4: Extinction du son, de 5 à 10: formation du conditionnement du son aigu, 11: géneralisation, de 21 à 29: différenciation, 30 et 31: contrôle d'extinction.

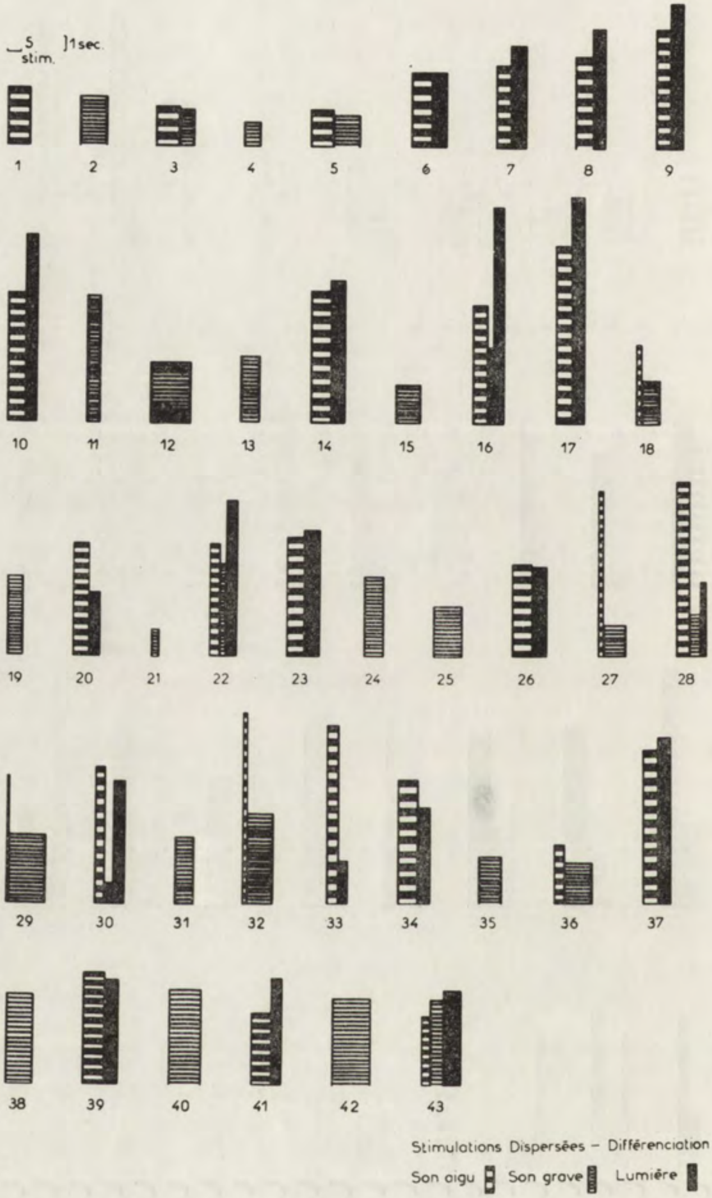


Fig. 12. Série de 43 expériences de différenciation par la méthode dispersée chez le lapin. Colonnes à bandes noires et blanches: son aigu, colonnes à hachures: son grave, colonnes noires: lumière. L'épaisseur des colonnes correspond au nombre des stimulations appliquées pendant l'expérience, la hauteur à la moyenne des durées des réactions d'arrêt correspondantes. De 1 à 5: extinction du son, de 6 à 10: formation de l'acquisition, 11: généralisation, de 27 à 36: différenciation, de 38 à 43: disparition de la différenciation

sont à peu près égales aux réponses au son grave. Quoiqu'il en soit le groupement des séances où sont présents à la fois le son aigu et le son grave permet de comparer terme à terme les résultats obtenus au cours du conditionnement différencié (fig. 11) et au cours de la différenciation par la méthode dispersée (fig. 12). Cette comparaison effectuée par le calcul du U de Mann et Whitney met en évidence des différences significatives à $p<0.001$ entre le son aigu et le son grave quelle que soit la méthode de distribution des stimulations; ces différences pouvaient déjà être prévues par l'examen des moyennes dont les chiffres sont respectivement de 10 et de 3,6 pour le son aigu et le son grave de la différenciation classique, et de 11,9 et de 4,5 dans le cas de la différenciation par la méthode dispersée.

Chez l'Homme. Les 2 sujets choisis pour ces longues séries d'expériences présentent un tracé EEG caractérisé par des réactions d'arrêt conditionnées stables et relativement brèves. L'un d'eux a subi 34 séances de différenciation conditionnée, l'autre 33 séances de différenciation par la méthode dispersée.

Les résultats obtenus avec ces deux méthodes sont figurés dans le tableau de la figure 13. Le calcul du U de Mann et Whitney met en évidence des différences significatives entre les réponses au son aigu et les réponses au son grave, différences que laissaient prévoir l'examen des moyennes qui sont respectivement de 12,9 et de 5,6 pour la différenciation classique, de 6,3 et de 2 pour la différenciation dispersée.

Ces résultats confirment que chez le lapin comme chez l'homme l'application de stimulations suivant un protocole particulier aboutit à une différenciation entre les réponses au son aigu et les réponses au son grave quelle que soit la méthode d'association utilisée, méthode des combinaisons ou méthode dispersée.

DISCUSSION

Les analogies très apparentes existant entre les réponses acquises par la méthode dispersée et les réponses conditionnées soulèvent deux principaux problèmes concernant d'une part, la spécificité de ces acquisitions, d'autre part, leur éventuelle identité.

I. *Spécificité des acquisitions conditionnées et dispersées.* La problème de la spécificité des réponses acquises est étroitement lié à la définition même du conditionnement. On sait que le réflexe conditionné se distingue du réflexe inconditionné par son aspect plus élaboré qui se manifeste notamment dans le conditionnement de type II (Konorski 1948) et surtout par son électivité d'apparition à la suite d'un stimulus déterminé tandis qu'un stimulus voisin reste sans effet. Or, ces caractères très précis semblent se retrouver dans les réponses acquises par la méthode dispersée.

Aspect de la réponse. Au premier abord l'emploi de la réaction d'arrêt EEG comme témoin d'une acquisition paraît discutable, et certains auteurs, rappelant que cette réponse est provoquée par le son avant toute association, considèrent le conditionnement EEG en général comme la simple réactivation d'une réponse d'orientation. En fait, la réaction d'arrêt conditionnée diffère de la réaction d'arrêt contemporaine de la réaction d'orientation par son siège plus limité (Mushkina 1956, Gastaut et al. 1957), et dans le cas particulier du conditionnement au son et à la lumière, par sa durée plus longue. Dans ce type de conditionnement en effet, la réaction d'arrêt conditionnée au son est suivie d'une action prolongée, marquée par des réactions d'arrêt successives qui caractérisent habituellement la réponse à la stimulation lumineuse (Popov 1953).

Nous avons retrouvé tous ces éléments présents dans les réponses acquises par la méthode dispersée et aurions pu même prendre comme témoin de l'acquisition chez le lapin et chez l'homme, l'action prolongée EEG. Cette réponse est cependant plus difficile à mesurer car au moment de sa terminaison, elle se confond avec l'aspect du tracé spontané qui réapparait (fig. 2 et 3). C'est la raison pour laquelle nous avons préféré prendre pour critère la réaction d'arrêt initiale.

Différenciation. La différenciation obtenue par la méthode dispersée paraît évidente mais le protocole expérimental employé pour l'obtenir s'écarte sensiblement des schémas de la différenciation Pavlovienne et pourrait évoquer soit une extinction chronique, soit une désinhibition par agent externe ou encore une différenciation immédiate mais non conditionnée.

L'extinction chronique, fréquemment utilisée par Konorski (1948) consiste, après avoir conditionné plusieurs stimuli, à répéter successivement chacun d'eux seul dans des séances d'extinction, pour apprécier la force respective des liasons conditionnées, l'extinction étant d'autant plus rapide que cette liaison est plus faible. C'est ce qui est pratiqué ici dans les séances où le son grave est répété seul. Cependant à l'opposé des stimulations dont on recherche l'extinction chronique le son grave des séances de différenciation dispersée n'a pas été associé auparavant avec la lumière. Par ailleurs, la suite de l'expérimentation qui réunit dans une même séance le son aigu et le son grave se sépare du protocole de l'extinction chronique.

Plus frappante est la ressemblance entre certaines séances de différenciation dispersée et les expériences de Pavlov (1929) destinées à mettre en évidence une désinhibition au moyen d'un „agent externe". En effet, lorsque le son aigu est intercalé dans une séance de sons graves, il provoque une réaction d'arrêt de longue durée contrastant avec l'absence de réactions d'arrêt aux sons graves et qui peut traduire soit un processus de différenciation, soit une réponse nouvelle liée à l'intervention d'un agent étranger à l'expérience et provoquant d'après les données Pavlovienne une „désinhibition de l'extinction du son grave". Un tel phénomène paraît intervenir dans l'expérience (Varga et Pressman 1961) de la figure 10 où le son aigu N° 420 déclenche la réapparition d'une réaction d'arrêt au son grave N° 421. Mais ce phénomène n'est pas constant et, dans plusieurs expériences chez l'homme, une réponse forte au son aigu reste isolée au milieu de réponses faibles ou nulles aux sons graves. De toutes façons la notion de désinhibition par agent externe ne peut s'appliquer aux résultats de certaines expériences (figure 10 expérience 24) où le son grave, introduit dans une séance de stimulations dispersées, donne au contraire, des réponses inférieures aux réponses au son aigu. Dans ce cas une différenciation vraie paraît être en cause.

Il n'en reste pas moins que la différenciation obtenue à l'aide de stimulations dispersées persiste moins longtemps que la différenciation conditionnée et tend à disparaître chez l'animal comme chez l'homme avec la répétition des séances, mais cette labilité relative de la différenciation dispersée ne s'oppose pas aux caractères fondamentaux de la différenciation Pavlovienne (Pavlov 1929).

Il semble donc bien que la méthode dispersée puisse aboutir à la formation de réponses acquises dont la spécificité ne correspond pas à ce qui est décrit dans la dominance et le pseudoconditionnement. C'est pourquoi nous appellerons „acquisition libre" cette association réalisée sans distribution ordonnée des stimulations par opposition au conditionnement qui nécessite un ordre chronologique rigoureux dans la combinaison des stimulations. Bien qu'elle soit „libre", cette acquisition suppose, du moins dans les expériences EEG, une contrainte imposée par convention et fondée sur l'aspect du tracé. Cette contrainte, qui revient à n'effectuer d'expériences que sur des sujets présentant un état de vigilance déterminé, n'empêche pas de faire varier l'ordre des stimulations ni les intervalles de temps qui les séparent. Cette dispersion des stimulations dans le temps constitue pour nous le principal élément du caractère „libre" de l'acquisition.

II. *Identité ou disparité de l'acquisition libre et du conditionnement.* Les analogies très frappantes observées entre l'acquisition libre et le conditionnement amènent à poser le problème de l'identité possible de ces deux modes d'association et à considérer par exemple l'acquisition libre comme un phénomène déjà décrit dans le réflexe conditionné classique, qu'il s'agisse du conditionnement à l'ambiance, du conditionnement au temps, du conditionnement à la séquence, du conditionnement à la trace ou du conditionnement à renforcement différé.

Dans le cas du conditionnement à l'ambiance la réponse conditionnée n'est pas déterminée par les stimulations mais par l'ambiance expérimentale. Ce phénomène ne semble pas être en cause dans les expériences EEG, car le conditionnement à l'ambiance y est lisible sur le tracé et se manifeste par des séries de réactions d'arrêt successives apparaissant sporadiquement. Une surveillance constante de l'enregistrement permet de n'appliquer les stimulations qu' au moment où le tracé EEG à repris son aspect de base, et de s'assurer que les réponses sont bien provoquées par les stimulations et non par l'environnement.

Une autre forme dégradée de conditionnement est le conditionnement au temps dans lequel la stimulation déclenchante n'est pas le stimulus conditionné mais la fixité des intervalles de temps séparant les stimulations. La réponse survient alors même en l'absence de stimulations, au moment où la stimulation suivante devrait être appliquée. Ce phénomène apparaît très précocément sur le tracé EEG puisqu'il suffit d'appliquer 3 ou 4 stimulations lumineuses à des intervalles de temps égaux pour voir apparaître, après un même intervalle, une réaction d'arrêt spontanée sur le tracé. Mais l'obligation posée par principe, de ne donner des stimulations qu'au moment où le tracé reprend son aspect de base, permet d'éviter ce conditionnement au temps qu'une deuxième précaution, consistant à faire varier constamment les intervalles de temps entre les stimulations, parvient probablement à éliminer.

C'est une précaution du même ordre qui permet d'écarter la possibilité du conditionnement à la séquence. Dans ce mode particulier d'association la réponse conditionnée est liée à la présence de séquences stéréotypées (par exemple dans le cas du conditionnement son-lumière S, S, SL, SL, S, S, SL, SL, S, S) et non au stimulus conditionné. Il en résulte que l'application à la place du son S d'une stimulation quelconque S, ou SL, ou S2 ou même L peut entraîner l'apparition de'une réponse habituellement provoquée par S. Un tel phénomène a pu être évité dans nos expériences du fait de l'absence de séquences stéréotypées et d'une répartition de stimulations apparentée à une distribution au hasard.

Quant au conditionnement à la trace qui peut apparaître même si un intervalle de temps important sépare le stimulus conditionnel du stimulus inconditionnel, il suppose cependant que cet intervalle soit fixe, au moins pendant une partie de l'expérience, ce qui n'est pas le cas ici.

Plus difficile est le problème posé par le conditionnement à renforcement différé, où l'application du stimulus inconditionnel succède à la distribution d'une série de stimuli conditionnels. L'expérience montre que dans ce cas le conditionnement se forme facilement et que chacun des stimuli de la série provoque une réponse conditionnée. L'acquisition libre où se succèdent des séries de 1,2 ou 3 stimuli in conditionnels et des séries de 1,2 ou 3 stimuli conditionnels rentrerait alors dans le cadre de ce conditionnement, mais il faut souligner que le conditionnement à renforcement différé met en jeu un ordre chronologique rigoureux des stimulations qui est absent dans l'acquisition libre.

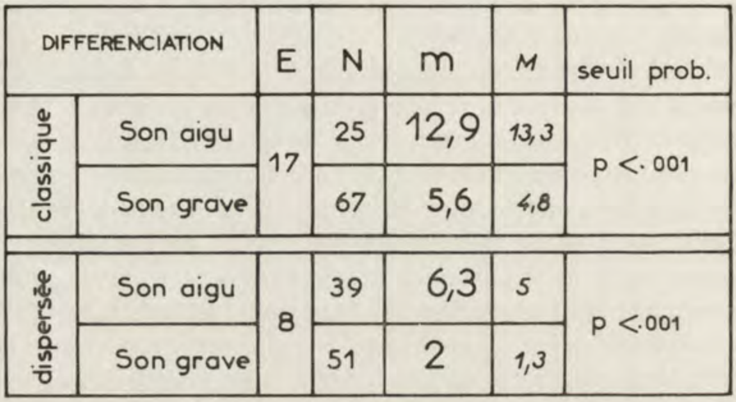
En fait le problème de l'identité ou de la disparité de l'acquisition libre ou du conditionnement repose essentiellement sur l'importance qui doit être attachée à l'ordre chronologique des stimulations. Dans le cas du conditionnement cet ordre est respecté, le stimulus conditionnel précède le stimulus inconditionnel d'un intervalle de temps déterminé. Dans l'acquisition libre tout se passe comme si „un garçon de Laboratoire faisait preuve de négligences dans son métier" et comme si en dépit de ces négligences, l'animal réalisait tout de même l'association. Le garçon objectera que de toutes façons un facteur chronologique est présent, qu'il ne concerne plus les stimulations mais l'ensemble de l'expérience et que, même si la dispersion des stimulations les répartit dans des séances successives, comme cela arrive dans les expériences de dominance, deux stimulations ne sont plus indépendantes à partir du moment où elles sont appliquées chez le même animal.

Il n'en reste pas moins que les faits décrits ici amènent à dissocier dans toute acquisition deux mécanismes qui semblent parfois confondus:

Le premier, très apparent dans le conditionnement, consiste dans la reproduction d'une sèquence de stimulations. A cet égard tout conditionnement serait un conditionnement à la séquence puisqu'il fait se succéder de la même façon et avec le même intervalle de temps deux stimulations. C'est sur ce point qu'a insisté Popov (1929) en décrivant la cyclochronie comme „une aptitude à reproduire les excitations précédentes dans l'ordre temporel même où ces excitations ont été provoquées auparavant par les stimulations correspondantes".

Le deuxième mécanisme a généralement été considéré comme l'expression d'une dominance survenant au moment de la phase de „généralisation" qui accompagne la formation du réflexe conditionné. A ce moment écrit Pavlov: „Le centre du réflexe absolu devient comme le point d'attraction pour les excitations qui viennent des autres surfaces d'excitation" et Popov (1929) met en parallèle la définition de Uchtomski (1950) considérant la dominance comme le „foyer d'excitation qui attire à lui les vagues d'excitation de différentes sources". Il paraît probable qu'au moment de la généralisation, alors que n'importe quelle stimulation est susceptible de provoquer le réflexe inconditionné, le facteur chronologique ou cyclochronique n'est pas mis en jeu car ces différentes stimulations n'ont jamais été combinées de façon rigoureuse ni ordonnées avec le stimulus inconditionnel.

Mais un tel fait n'autorise pas à conclure que la suppression de ce facteur chronologique supprime l'association ou l'entraîne nécessairement vers des niveaux d'acquisition inférieurs, où elle devient grossière, émotionnelle, ,,pseudoconditionnée''. Au contraire les faits décrits dans cette étude montrent qu'une association de ce type, en dépit de l'absence de facteurs chronologiques rigoureux, peut se révéler spécifique et élective.



DIFFERENCIATION		E	N	m	M	seuil prob.
classique	Son aigu	17	25	12,9	13,3	p <·001
	Son grave		67	5,6	4,8	
dispersée	Son aigu	8	39	6,3	5	p <·001
	Son grave		51	2	1,3	

Fig. 13. Comparaison de la différenciation classique et de la différenciation par la méthode dispersée chez l'homme. E = nombre d'expériences où sont présentes de son aigu et le son grave. N = nombre de stimulations. m = durée moyenne des réactions d'arrêt. M=Médiane. Avec la méthode classique comme avec la méthode dispersée, la différenciation est marquée par des chiffres deux ou trois fois plus élevés pour le son aigu que pour le son grave.

Ces caractères nous ont paru présents au cours de l'observation dans le Laboratoire du Professeur Konorski de quelques réflexes alimentaires instrumentaux chez le chien par la méthode dispersée. Les réflexes acquis par cette méthode étaient fins, hésitants, fragiles et paraissent traduire une élaboration plus complexe que les réflexes conditionnés dont le déroulement plus régulier et plus stable évoquait une activité plus automatique. Ces observations ne constituent pas une expérimentation et il est peut-être prématuré d'individualiser dès à présent à l'aide d'arguments exclusivement électrophysiologiques une ,,acquisition libre'', capable de relier des événements indépendants, et qui serait à l'intuition et à certaines expériences sociales ce que le conditionnement est à l'acquisition scolaire ou à la formation militaire.

Cependant, le fait qu'une association puisse relier spécifiquement les effets de deux stimulations qu'elles soient rigoureusement couplées ou au contraire dispersées amène à assouplir et à élargir la définition du réflexe conditionné classique.

Nous remercions Mme Combe et Mlle Trinson qui nous ont exécuté les schémas.

RÉSUMÉ

Une étude EEG utilisant le son comme stimulus neutre et la lumière comme stimulus inconditionnel est effectuée chez l'animal et chez l'homme.

Deux méthodes d'application des stimulations sont utilisées: la première est basée sur la combinaison des stimulations qui sont données par couples comme dans le conditionnement classique, la seconde sur la séparation de la lumière et du son qui sont distribués séparement à des intervalles de temps variables et sans ordre particulier.

De nombreux caractères communs sont observés pour les réponses acquises par ces deux méthodes: apparition, variations typologiques chez l'homme, extinction... Bien plus une différenciation des réponses au son aigu et au son grave peut être mise en évidence chez l'animal et chez l'homme, non seulement dans les séances de conditionnement, mais, à l'aide d'un protocole expérimental particulier, dans les séances de stimulations dispersées. Ces résultats amènent à discuter l'existence, à côté du réflexe conditionné classique, d'une acquisition „libre" et pourtant spécifique capable de relier des stimulations indépendantes ou tout au moins non ordonnées dans le temps.

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„INHIBITION OF DELAY" AS A MECHANISM OF THE GRADUAL WEAKENING OF THE CONDITIONED EMOTIONAL RESPONSE[1]

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In several experiments involving comparatively long training of the conditioned emotional response (CER), a U-shape acquisition curve was observed: within the first few days of training Ss acquire a fairly profound suppression while on later days an upward drift of suppression ratios was observed (Kamin 1961, Annau and Kamin 1961, Kamin and Brimer 1963). As a possible explanation of these results an „adaptation" to the US in the course of the CER training was mentioned (Annau and Kamin 1961). However, other mechanisms causing the U-shape of the CER acquisition curve are possible.

First of all, long CS—US intervals commonly used in CER studies may provide conditions for development of so-called „inhibition of delay". Such a phenomenon was repeatedly observed in Pavlovian Laboratories. Shaping of the conditioned salivation reflex was done with short CS—US intervals. Then, the CS—US interval was prolonged to provide the opportunity to measure more precisely the amount of conditioned salivation. After some period of training with long CS—US intervals, only rudimen-

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tal outflow of saliva was observed in the beginning of the action of the CS, and the CR in full strength appeared toward the end of the CS—US interval (Zavadskii 1908). The diminution of salivation within the first period of the CS—US interval was considered as a result of acquisition of an active process of inhibition (Pavlov 1932, Konorski 1948).

The method of establishing inhibition of delay by transformation of the CR with short delay to that with long delay was used in a variety of species also for instrumental conditioned reflexes (Baru 1962, Ivanova 1963, Krasuskaia and Pavlov 1962, Pavlov and Saf'iants 1962, Prazdnikova 1962, Chebykin 1962, and others). However, there is little information whether or not the inhibition of delay can develop when a long CS—US interval of constant duration is used from the very beginning of training. If this process occurs, one may expect a gradual shift of the fear response toward the end of the CS—US interval in the course of CER training. In consequence, the suppression of the bar-pressing response will be less in the beginning of the CS—US interval than toward the end.

Another possible mechanism causing decrease of suppression with overtraining is a consequence of the food reinforcement schedule used to mantain the bar-pressing behavior. If the variable interval (VI) schedule is used, the probability of reinforcement of one particular bar press is related to the rate of responding in the preceding period of time. Let us consider a limiting case, when full suppression of the bar-pressing during the action of the CS is observed. With long CS—US interval and relatively short variable interval of food reinforcement, *the first* bar press after the CS—US period will be reinforced with food. Thus, the CS offset and/or the shock application may become to be signals for high probability of food reinforcement. It has been shown that due to differential pairing of shock with food reinforcement the shock itself may increase responding in an operant behavior situation (Holz and Azrin 1961). The Ss may also learn that after long non-pressing the bar-pressing response is more effective (Skinner 1938). This would lead to the occurrence of bar presses in the end of the CS—US interval. These forms of learning may be eliminated by use of the VI „limited hold" (LH) schedule. In this schedule the food reinforcement is „waiting" for a bar-pressing response only a fixed length of time, and then, if the response does not occur, reinforcement is omitted and the new between-reinforcement interval started. In such a procedure long non-responding does not change the probability of food reinforcement for the one bar press (Ferster and Skinner 1957).

All mechanisms mentioned above give the same result in terms of an upward drift of over-all suppression ratios. However, a detailed analysis of the distribution of bar-presses during the CS—US interval and rate of responding just after the US application may throw same light on the mechanisms causing the U-shape of the CER acquisition curve.

MATERIAL AND METHODS

The Ss were 20 experimentally naive male hooded rats from the McMaster Univ. colony, approximately 5,5 mo. of age at the beginning of the experiment. Five standard Grason-Stadler operant conditioning units were used in the experiment. The apparatus and method of shaping of the bar-pressing response for food were experiment except for the food reinforcement schedule used to mintain bar-pressing response during the first day of training was followed by three daily 2-hr. sessions of bar-pressing under a 2.5 min VI food-reinforcement schedule. The actual series of intervals between consecutive reinforcements was 12, 42, 126, 366, 234, 24, 168, 66, 90, and 288 seconds. The reinforcement was standard 45 mg. Noyes food pellets. After the third day of training with 2.5 min VI schedule, Ss were split into two experimental groups, 10 Ss each (due to middle-ear infection Group 2 was reduced to 9 Ss). Both groups had exactly the same treatment in all stages of the experiment except for the food reinforcement schedule used to maintain bar-pressing behavior. For Group 1 the regular 2.5 min VI schedule was used throughout the whole experiment. For Group 2 the 2.5 min VI LH schedule was used: after variable intervals with mean of 2.5 min duration, the food reinforcement was available for only 20 secs, and if the S did not press the bar during this period, a clock was reset and a new variable interval started.

Three additional sessions of bar-pressing training were given before the stimuli used for CER training were introduced. The CS was a white noise of 80 db intensity presented during each 2-hr. session three times for 6 minutes each time. The onsets of the stimuli were at 22, 57, and 85 min after the beginning of the session. On the day following preliminary training CSi were presented in the appropriate time without shock application. This session constituted so called Pretest day. Then CER training began and continued for 21 days. During this stage of the experiment each offset of the CS coincided with a .85 ma. shock of .5 sec duration.

Measures. For each trial numbers of bar presses were counted independently for three 2 min periods before the CS onset (pre-period), for three 2 min periods during the action of the CS (CS-period), and for 2 min period after the CS offset (post-period). The magnitude of the CER was measured by computing the „suppression ratio" described by Annau and Kamin (1961). The ratio is $\frac{B}{A+B}$ where B represents number of bar presses emitted during the 6 min CS-period, and A-number of bar presses during 6 min pre-period.

„Daily" ratios were computed for each S by summating responses during the appropriate time intervals of three trials in a single session. Pattern of responding during the CS—US interval was investigated by comparing numbers of responses emitted in three consecutive 2 min time periods, which will be denoted as B_1, B_2, and B_3. Effect of the CS offset and shock application on bar-pressing response rate was studied by comparing numbers of responses emitted during the 2 min periods just preceding the CS onset and just following the CS offset. In each case, when numbers of bar presses emitted during given time intervals ware subjected to the analysis of variance, the Freeman-Tukey square-root transformation of the raw data was used (Meredith and Wong 1961).

RESULTS

Changes of the suppression ratios. In accordance with previous observations (Zieliński 1965) the first application of the 80 db white noise during the Pretest day caused only a shortlasting inflection of the bar-pressing response rate. Median ,,daily''suppression ratios computed for the Pretest day equal .51 for each experimental group.

The CER acquisition was very rapid. Already by the 1st trial of the 2nd day of CER acquisition (the 4th trial from the beginning of training) the CS evoked significant suppression in both experimental groups ($p < .05$ in Group 1, and $p < .02$ in Group 2). This was shown by a comparison of the number of bar presses emitted during the pre-period and the CS-period

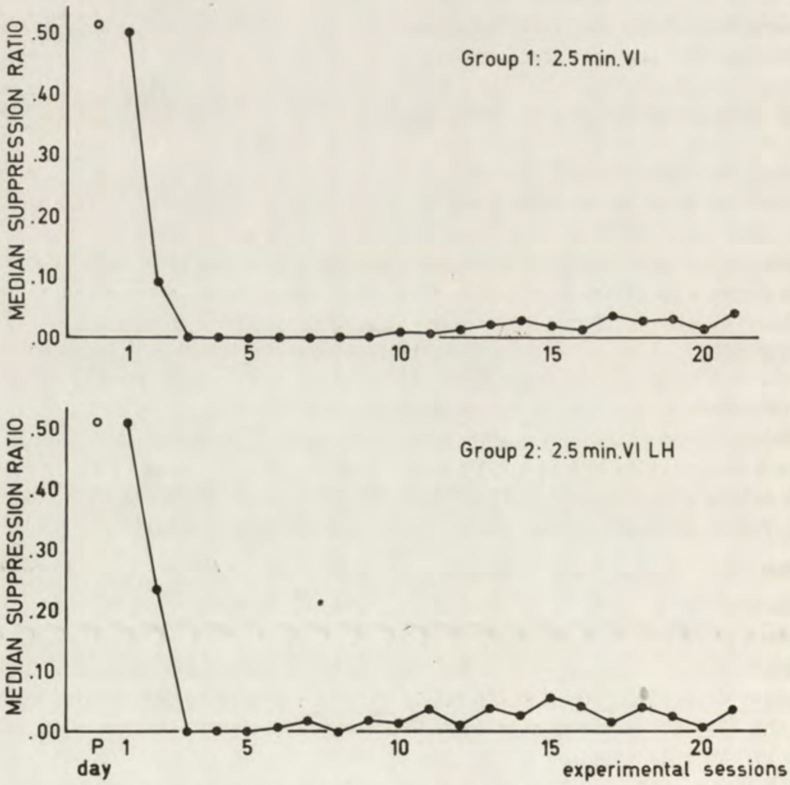

Fig. 1. Median daily suppression ratios during the P-day and the CER acquisition.

for a given trial using the Wilcoxon matched-pairs test, two tailed (Siegel 1956). At the 3rd day of the CER acquisition median suppression ratios reached nil in both groups. Then a slight upward drift of the suppression ratios was noticed, as seen from Fig. 1. To test whether or not this upward drift of the suppression ratios was statistically significant, daily suppression ratios in 2—21 sessions of the CER acquisition were analysed. These twenty sessions were split in four blocks, five sessions each. For each S four median daily suppression ratios, which characterize the level of suppression in consecutive blocks were estimated. Then, the method of nonparametric trend analysis suggested by Fergusson (1965) has been applied to these median suppression ratios[3]. From this analysis there is evident a marked monotonic increasing trend significant at $p<.001$ level in each experimental group.

Pattern of responding during the CS—US intervals. Pattern of responding during the CS—US intervals was investigated in a following way. Within each block of 5 training sessions there were 15 presentations of the CS. Within a given block of sessions sums of the numbers of responses emitted during all B_1, B_2, and B_3 periods independently were calculated for each S. Means and medians obtained from these data are presented for each experimental group in Table I. From these data it is evident that

Table I

Numbers of responses emitted per minute in three consecutive 2 min periods (B_1, B_2, and B_3) of the CS—US interval on different stages of the CER training

Experimental group and Stage of training	Mean			Median		
	B_1	B_2	B_3	B_1	B_2	B_3
Group 1: 2.5 min VI						
2 — 6 sessions	1.43	1.29	1.57	.20	.08	.16
7 — 11 sessions	.06	.54	.70	.10	.00	.00
12 — 16 sessions	1.26	.48	.61	.18	.00	.03
17 — 21 sessions	1.87	.81	.84	.40	.03	.03
Group 2: 2.5 min VI LH						
2 — 6 sessions	.62	.70	.60	.23	.26	.26
7 — 11 sessions	.53	.33	.48	.07	.03	.17
12 — 16 sessions	1.49	.85	.84	.27	.33	.33
17 — 21 sessions	1.70	.63	.72	.33	.00	.10

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[3] The method developed by G.A. Fergusson 1965 employs the S statistics as used by Kendall in the definition of a coefficient of rank correlation, *tau*. The null hypothesis was tested against the two-tailed research hypothesis that a monotonic (increasing or decreasing) trend in amount of suppression over consecutive blocks of experimental sessions exists.

the lowest level of responding was observed during the second block of the training sessions. In next blocks the level of responding increased, however, only during the first 2 min of the CS—US interval. When the Fergusson's trend analysis was applied to these data, it was shown that during four blocks of sessions the monotonic increasing trend of the numbers of bar presses emitted during the B_1 period was observed ($p<.005$) and no systematic changes for the B_2 and B_3 occurred. Actually, the numbers of bar presses emitted during the B_2 and B_3 periods have tendency to decrease in the course of training.

The Friedman two-ways analysis of variance by ranks (Siegel 1956) was used to estimate the statistical difference between response rates in consecutive B_1, B_2, and B_3 periods. The analysis was done independently for each block of training sessions and experimental group. Scores, which characterize level of responding, were ranked for each S separately, the rank 1 was given to the lowest level of responding, and the rank 3 — to the highest level of responding. Mean ranks for each experimental group and block of sessions are presented in Table II. The Friedman test has shown that ranks do not differ during the first three blocks of training sessions and they do differ significantly during the last block of sessions ($p<.05$ for the Group 1 and $p<.001$ for the Group 2). From the data presented in Table II it is evident that the highest level of responding was observed in the beginning, and the lowest level of responding — in the middle of the CS—US interval.

Table II

Mean ranks, which characterize consistency of the pattern of responding in three consecutive 2 min periods (B_1, B_2, and B_3) of the CS—US interval in different subjects of a given experimental group

Experimental group	Stage of training	B_1	B_2	B_3
Group 1: 2.5 min VI	2 — 6 sessions	2.4	1.6	2.0
	7 — 11 sessions	2.2	1.6	2.2
	12 — 16 sessions	2.5	1.6	1.9
	17 — 21 sessions	2.6	1.5	1.9
Group 2: 2.5 min VI LH	2 — 6 sessions	1.7	2.2	2.1
	7 — 11 sessions	2.5	1.6	1.9
	12 — 16 sessions	2.6	1.5	1.9
	17 — 21 sessions	3.0	1.2	1.8

As seen from the Table III, the changes of the pattern of responding during the CS—US intervals in the course of training were the same in the two experimental groups (analysis of variance, mixed design, type VI — Lindquist 1953). Here, the numbers of responses emitted by each S during the B_1, B_2, and B_3 2 min periods within each 5 sessions block were used as raw data. The differences between blocks, the 2 min periods, and effect of the interaction of these two factors were confirmed by this analysis.

Table III

Results of the analysis of variance (mixed design, type VI — Lindquist 1953) of the numbers of bar presses emitted during the consecutive 2 min periods and blocks of sessions in the two experimental groups

Source of variation	df	MS	F
Total	227	60.04	—
Between-Subjects	18	567.60	—
Groups (C)	1	7.82	< 1
Error (b)	17	600.52	—
Within-Subjects	209	16.32	—
Blocks (A)	3	102.55	3.29*
2 min periods (B)	2	164.21	13.49**
AB	6	34.57	8.17**
AC	3	36.91	1.18
BC	2	4.39	< 1
ABC	6	1.85	< 1
error$_1$ (w)	51	31.21	—
error$_2$ (w)	34	12.17	—
error$_3$ (w)	102	4.23	—

* denotes effect significant at the $p < .05$ level.

** denotes effect significant at the $p < .001$ level.

Bar-pressing rate before and after the CS—US interval. Here, the number of bar presses emitted during the 2 min period immediately preceding the CS onset and the number of bar presses during the 2 min period immediately followed the CS offset were analysed. The sums of the number of bar presses calculated for each 2 min period, block of the 5 consecutive sessions, and S independently were used as raw data. Analysis of these data for the 2nd-21st sessions has shown that the level of responding increased in consecutive blocks of sessions ($p < .001$), and it was higher before than after the action of the CS ($p < .01$). No group differences were observed and no one interaction term reached significance (analysis of variance, mixed design, type VI). The differences between rates of responding before and after the action of the CS, as well as increase of the rate in consecutive blocks of sessions were rather small, but, as seen from Table IV quite consistent.

Table IV

Numbers of responses emitted per min. during the 2 min. periods immediately before (A) and immediately after (C) the action of the CS on different stages of the CER training

Experimental group and Stage of training	Mean		Median	
	A	C	A	C
Group 1: 2.5 min VI				
2 — 6 sessions	7.6	5.9	7.7	6.0
7 — 11 sessions	6.8	6.2	6.2	5.4
12 — 16 sessions	8.1	7.2	6.8	6.7
17 — 21 sessions	8.7	7.4	7.0	7.0
Group 2: 2.5 min VI LH				
2 — 6 sessions	5.7	4.6	7.0	4.0
7 — 11 sessions	5.9	4.8	6.0	5.6
12 — 16 sessions	7.0	6.1	7.4	7.2
17 — 21 sessions	7.6	6.0	7.6	6.3

DISCUSSION

The data presented in this paper clearly demonstrate that the observed diminution of the suppressing properties of the CS paired with shock on the on-going bar-pressing behavior may be explained as a result of development of „inhibition of delay”. It has been shown that the increase of the number of bar-presses in the course of training was restricted only to the beginning of the CS—US interval, which indicates weakening of the fear response in the beginning and not in the end of the CS—US interval. The observed changes of the pattern of responding within the CS—US interval can not be predicted on the basis of the „adaptation” hypothesis, which postulate general weakening of the suppressing effect of the CS paired with an unavoidable shock.

However, the term „inhibition of delay” is devaluated now, because it was incorrectly used in a number of papers to describe different phenomena occurring during training of long-delayed CRs. The long CS—US interval used from the very beginning of training may have at least three different effects. We will list them.

1. The longer is the temporal span between the CS and the US onsets, the more difficult is the course of conditioning. This results in a small probability of the conditioned response which increases during training. As latency of the conditioned response is one of the measures of the strength of conditioning, the latencies would be long in the beginning and

become shortened during training (Behrend and Bitterman 1962, 1964).

2. If we assume that the afferent state of affairs existing immediately before the application of the US serves as the conditioned stimulus, temporal discrimination may be observed at the same time when the first conditioned responses occur and thus long latency of the CR is observed from the very beginning. Even if latencies of the CRs change slightly during the further training, short-latency CRs may never be observed when long CS—US intervals are used (Kamin 1954, Brush et al. 1955, Church et al. 1956, Church and Black 1958, Pavlov and Saf'iants 1962, Bitterman 1964).

3. The process leading to development of inhibition of delay is, according to Pavlovian theory, experimental extinction, because early phases of the CS „do not fit in closely with the time of appearance of the unconditioned stimulus" (Pavlov 1932, p. 93). Thus, we may speak, about inhibition of delay only in these cases, when at first, both early and later phases of the CS possess excitatory properties, and then, in the course of training the early phases of the CS lose partially or completely these properties, whereas later phases of the CS evoke the CR as before. Thus, latencies of the conditioned responses are short in the beginning and they lengthen in the course of training. Such development of „inhibition of delay" was routinely observed after transformation of shortly delayed CRs to those with long CS—US intervals. Only in the present experiment and in one dog trained in a variation of the avoidance reflex by Ivanova (1963) was observed inhibition of delay in conditions of a long constant CS—US interval. In other three Ss trained by Ivanova, shaping of inhibition of delay without gradual prolongation of the CS—US interval was preceded by training of shortly delayed CRs to other CSi.

Thus, these data demonstrate that transformation of shortly delayed CRs to those with long delay is not a necessary condition for the development of „inhibition of delay", but this phenomenon may occur with CS—US intervals of constant duration from the very beginning of training. Such an outcome occurs, when conditioning of the reflex studied is possible with long CS—US intervals. The „conditioned emotional response", opposite to the conditioned salivation reflex, belongs to the class of reflexes easily conditionable with the temporal span between the CS and the US onsets lasting even several minutes.

In the present experiment the effect of the food reinforcing schedule was negligible. In spite of the fact that Ss trained with the 2.5 min VI LH schedule obtained only about 80 per cent of food pellets available by those trained with 2.5 min VI schedule, the two experimental groups did not differ neither in bar-pressing rate during intertrial intervals, nor in amount of suppression and in pattern of responding during the CS—US intervals. In both groups rate of responding was higher before the CS onset than after the CS offset.

Compensatory increase of the rate of responding following the CS—US interval, described by Estes and Skinner (1941), was not observed in the present experiment. Thus, we may conclude that the only mechanism causing the upward drift of the suppression ratios during the CER training was in the present experiment development of the inhibition of delay.

SUMMARY

Changes of the pattern of responding within the CS—US interval during the CER training was studied in two groups of rats, which differed in regard to the food-reinforcing schedule used to maintain the on-going bar-pressing behavior. Both groups gradually acquired identical pattern of responding with greater numbers of bar presses in the beginning than toward the end of the 6 min. CS—US interval. Acquisition of this pattern of responding is considered as indicating development of „inhibition of delay" of the fear response.

Results of the present experiment demonstrate that „inhibition of delay" as a consequence of the gradual extinction of the excitatory properties of the early phases of the CS may develop, when long CS—US interval of constant duration is used from the very beginning of training.

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EXTINCTION OF A FOOD-REINFORCED RESPONSE IN RABBITS WITH LESIONS OF THE FRONTAL CORTEX

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It is now well established that behavioral changes which follow medial frontal cortex lesions in rabbits are reminiscent of those resulting from first the lateral and then the lateral as well as medial hypothalamic lesions (Brutkowski 1965, 1966, Balińska 1966, Balińska et al. 1966).

An earlier paper (Balińska et al. 1966) reported the finding that a bilateral damage to the medial frontal cortex, lateral hypothalamus and medial hypothalamus results in drive disinhibition. Lesions of the frontal cortex and lateral hypothalamus produce first hypoactivity and a reduction or abolition of conditioned-reflex (CR) performance and then a strengthening of the performance in company with a decreased ability to refrain from responding on nonreinforced trials[1]. On the other hand, lesions of the medial hypothalamus produce an increased reactivity and impairment of inhibition with no signs of an abolition or reduction of the performance at the early stages of the postoperative period.

Butter et al. (1963) have demonstrated that during extinction rhesus monkeys with orbital frontal lesions, unlike those with dorsolateral frontal lesions, perseverate a food-reinforced bar-pressing response. The purpose of the present study was to compare the effects on CR extinction of lesions of the medial frontal cortex (parts of which seem to be functionally comparable to the primate orbital frontal cortex, Brutkowski

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[1] Rabbits after lesions of the lateral hypothalamus were unable to feed themselves. However, they recovered their voluntary eating behavior when glucose with saline was injected subcutaneously for a few days postoperatively (Balińska 1963 b).

1965) and the dorsolateral frontal cortex in the rabbit. Recent work (Balińska and Brutkowski 1964) indicates that extinction of a food-reinforced response is much slower in lateral hypothalamic lesioned rabbits, who have regained eating behavior due to subcutaneous glucose and saline injections in the immediate postoperative period, than in medial hypothalamic lesioned rabbits still in the dynamic phase of hyperphagia.

MATERIAL AND METHOD

Subjects. The subjects were 6 rabbits, both males and females, 2 years old, weighing ca. 2.5 kg. They were maintained on ad-lib. diet, consisting of grains of oats, in individual cages.

Procedure. The testing cage and procedure were described elsewhere (Balińska 1963 a, b). All subjects were trained to pull with the teeth a ring located near the food box. Correct responses were reinforced with uniformly small pieces of carrot. The conditioned stimulus (CS) was a buzzer which went on 3 sec. and was presented 20 times per day at a 15-sec. intertrial interval, subtracting the time for eating the reinforcement food.

When the conditioned response to the presentation of the buzzer had been firmly established and the intertrial responding declined to zero the extinction training was begun. The extinction session followed the conditioning session every day. The sequence of treatments was as follows: (a) 20-trial conditioning session, and (b) extinction session during which the CS was presented for 3 sec. at an intertrial interval of 15 sec. until no response occurred to 10 successive presentations of the CS. This training was conducted to the criterion of one response in the extinction session within two consecutive days. After the criterion in extinction had been reached the animals were divided into two equal groups. One group received one-stage bilateral medial frontal lesions (group FM), and one, one stage bilateral dorsolateral frontal lesions (group FL).

Surgery and verification of lesions. A detailed description of the surgical procedure was given previously (Balińska et al. 1966). All animals were operated under aseptic conditions, using nembutal (40 mg/kg) anesthesia. The cortical removals were accomplished by suction. They consisted of the medially and dorsolaterally placed cortex in the FM and FL groups, respectively, on a 5-mm stretch, beginning at the tip of the frontal pole. At the end of testing all operated animals were sacrificed, and the brains removed. Estimates of lesion extent made from surface examination of the uncut brains revealed that all of the lesions were of the type described earlier (Balińska et al. 1966). Ten days were allowed before conditioning and extinction testing was resumed.

RESULTS AND DISCUSSION

Preoperative training. Conditioning. All animals learned to pull the ring to the presentation of the CS within several days. After the acquisition of this response many intertrial responses occurred. These showed a slow decrement during the course of training, but disappeared definitely only following a period of 6 to 8 weeks. The intertrial responses were consistently associated with strong emotional manifestations, such as stamping feet, violent turns, etc.

Extinction. As seen from Table I, all animals attained criterion within 5 to 8 days. During initial extinction sessions, clear-cut signs of excitement were noted: the animals stamped feet, explored excessively the testing cage, and tried to escape. Intertrial responding declined during training.

Table I

Number of extinction sessions to criterion before (A) and after (B) lesions of the frontal cortex in rabbits

Rabbit No.	A	B
Lesions of the medial frontal cortex, group FM		
1	6	18
2	6	18
3	8	21
Lesions of the dorsolateral frontal cortex, group FL		
4	7	2
5	8	2
6	5	2

Table II

Total number of intertrial responses during CR extinction before (A) and after (B) lesions of the frontal cortex in rabbits

Rabbit No.	A	B
Lesions of the medial frontal cortex, group FM		
1	29	113
2	24	115
3	39	120
Lesions of the dorsolateral frontal cortex, group FL		
4	26	2
5	36	2
6	28	2

Postoperative behavior. Group FM: General observations. Throughout a period of several postoperative days, all animals were hypoactive and showed obvious signs of motor incoordination with regard to feeding. They had difficulty in grasping food, exhibited marked disturbance in chewing and mastication, gnashed the teeth while eating, and ate considerably less comparing to the preoperative level. At least some of these defects, of course, might be attributable to an accidental damage to the premotor and motor regions of the brain.

Beginning with the second postoperative week, the operated animals had shown a marked evidence of improvement in motor and feeding behavior, which was followed by an increase in food-directed activity, characterized by intense sniffing and searching. In addition, all animals began to show an increased susceptibility to tactile stimuli. A violent aggressive-defensive reaction was elicited by touching an operated animal, or when attempts were made to take out the animal from the cage: the animal wriggled, escaped, or emitting squealing sounds, attacked one's hand extended. These emotional symptoms, which ware attributed to the damage to the cortical tissue located immediately in front of the genu of the corpus callosum (Brutkowski et al. 1961, Brutkowski and Wojtczak-Jaroszowa 1963, Brutkowski 1964, 1965), persisted for a period of many weeks. These observations are identical with those reported previously (Balińska et al. 1966).

Conditioning and extinction. At the early stages of postoperative testing, the pulling response occurred both to the presentation of the CS and during the intertrial interval within both conditioning and extinction sessions. It can be seen from Table II that all three animals of group FM made substantially more intertrial responses during extinction testing than did they preoperatively, or did the animals of group FL. Furthermore, it can also be seen from Table II that the FM animals suffered a marked deficit in the preoperatively acquired ability to extinguish the CR.

Excessive food-oriented activity occurred during both conditioning and extinction sessions. It slowly declined toward the end of the postoperative testing. There was an observable relationship between the tendency of an operated animal to show a strong food-oriented activity and a decreased ability to suppress the pulling response both on the extinction trial and during the intertrial interval. An improvement of extinction behavior and reduction of intertrial responding with further testing were clearly attributable to a decreasing strength of the food-directed activity in the later postoperative period.

These data are thus congruent with the hypothesis (Brutkowski 1964, 1965) that medial frontal cortex lesions in subprimates may increase an animal's emotional reactivity which would cause difficulty with suppression of the learned response on the nonreinforced trial.

Group FL: No abnormalities in either general aspects of behavior or conditioning and extinction relearning were detected in any of these animals (Tables I and II).

SUMMARY

Rabbits with lesions of the medial frontal cortex, unlike rabbits with lesions of the dorsolateral frontal cortex, showed decrements in extinction relearning. The finding that all rabbits with medial frontal cortex lesions showed substantial increase in food-directed activity was taken as evidence that excessive food-directed activity might interfere with suppression of the CR on the extinction trial. These results are consistent with the view that medial frontal cortex lesions in subprimates increase emotional reactivity which causes difficulty with the withholding of the learned response on the nonreinforced trial.

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Acta Biol. Exper. (Warszawa), vol. 26, No. 4, pp. 425—439, 1966

PREFRONTAL CORTEX CONTROL OF DIFFERENTIATION BEHAVIOR IN DOGS [1]

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Studies of the effect of frontal lesions on differentiation in the dog have shown that, under circumstances of reinforcing the positive conditioned reflex (CR) with food, acid or electric shock, a bilateral prefrontal lobectomy, including all brain tissue anterior to the presylvian and genual sulci on the lateral and medial aspects, respectively, of the cerebral hemisphere, is consistently followed by a temporary impairment or disinhibition of the previously established inhibitory CR (Konorski et al. 1952, Brutkowski et al. 1956, Szwejkowska et al. 1963, Brutkowski 1964, 1965).

Observations of the behavior of dogs with prefrontal lobectomies during differentiation performance suggest that an important factor in the impairment derives from the tendency of the operated dogs to increase their foodoriented responses in the situation in which food is presented on positive trials, or to augment their aggressive-defensive responses in the situation in which noxious reinforcements are used. Accordingly, it has

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[1] Short accounts of some of these findings have already been reported briefly at the meetings of the Czechoslovak Medical Congress on the occasion of the 100th Anniversary of the Foundation of the Czech Medical Association and the Czech Medical Journal, Prague, Czechoslovakia, November 12th—17th, 1962, and published in Science (S. Brutkowski and J. Dąbrowska: Disinhibition after prefrontal lesions as a function of duration of intertrial intervals), vol. 139, No. 3554, pp. 505—506, 1963.

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been concluded that an excess in drives accounts for the impairment of inhibition in animals with prefrontal lesions.

A further suggestion has been that excessive response perseveration, which is reported to occur in animals with damage to the frontal cortex, may interfere with the withholding of CRs on inhibitory trials. Since the disturbance in the ability to suppress CRs has first been established in animals with large prefrontal lobectomies, damaging regions possibly subserving different functions, it seems reasonable that both alternatives are valid, and that either of these two types of impairment of inhibition, that is, disinhibition of drives or disinhibition in terms of the perseveration of response may occur following selective lesions of one or the other parts of the prefrontal cortex. A differentiation task, consisting of successive presenting the positive and inhibitory conditioned stimuli (CSi) at short or long intertrial intervals (15, or 60 sec), was employed for this purpose (Brutkowski and Dąbrowska 1965). As a second purpose of this study, an effort was made to define the critical lesions in the dog's prefrontal cortex, producing a disinhibition.

MATERIAL AND METHOD

Subjects. The subjects were 37 adult male mongrel dogs. Their ages were indeterminate, but weights ranged from 8 to 12 kg. No animal had had previous experience in a formal training situation. All but one dogs were randomly assigned to the following experimental groups of four or eight each for purposes of surgery: L (lesion of the prefrontal cortex situated on the dorsolateral aspect of the hemisphere), M (lesion of the upper portion of the prefrontal cortex situated on the medial aspect of the hemisphere), P (lesion of the proreal cortex), AO (lesion of the anterior sector of the orbital gyrus cortex), PS (lesion of the cortex located within the inferior wall of the presylvian sulcus). SP (lesion of the lower portion of the prefrontal cortex situated on the medial aspect of the hemisphere). Group PO (lesion of the posterior sector of the orbital gyrus cortex) consisted of one animal since the posteroorbital gyrus cortex is relatively inaccessible surgically in the dog. Groups L, M and PS were divided into two subgroups of two or four animals each on the basis of the length of the intertrial interval: subgroup 1 was trained at 15-sec. intertrial intervals (L15, M15 and PS15), and subgroup 2 was trained at 60-sec. intertrial intervals (L60, M60 and PS 60). Groups P, AO, PO and SP were trained only at 15-sec. intervals (P15, AO15, PO15 and SP15).

Four dogs who had undergone a lesion of the posterior cingulate cortex served as control group (PC). Fig. 1 shows lateral and medial aspects of the dog brain indicating prefrontal regions.

Experimental procedure. The training and testing procedures were essentially similar to those described in detail by Brutkowski and Dąbrowska (1965) for the dog, and by Balińska et al. (1966) for the rabbit. The animals were trained to place the right forefood on the feeder in the presence of a positive CS (CS+), which was a 1000 cy/sec. tone and to withhold this response in the presence of an inhibitory CS (CS−), which was a 700 cy/sec. tone. On positive trials, food reinforcement occurred immediately following the placing response, or after 5 sec. if no response had been made. Thus food was presented on positive trials regardless of whether or not the CR was performed. The CS+ always overlapped a few seconds with the presentation of food. The CS− went on 5 sec. and was never followed by food reinforcement. The dogs received 15 positive and 15 inhibitory trials a day, each trial separated by a 15-sec. or 60-sec. interval. The CSi were presented in a prearranged random sequence. An error on positive trial consisted of not placing the forefoot on the feeder during 5-sec. presentation of CS+, while an error on inhibitory trial consisted of failing to withhold the placing response during 5 sec. of presentation of CS−. All subjects were trained to a criterion of 45 errorless inhibitory trials out of 50. Practically, no errors occurred on positive trials. A noncorrection technique was used throughout. Intertrial CR responses, which had occurred excessively at the early stages of differentiation training, disappeared definitely toward the end of preoperative training. Although primary consideration was given to the conditioned-reflex performance and inhibition, other overt behaviors were also recorded.

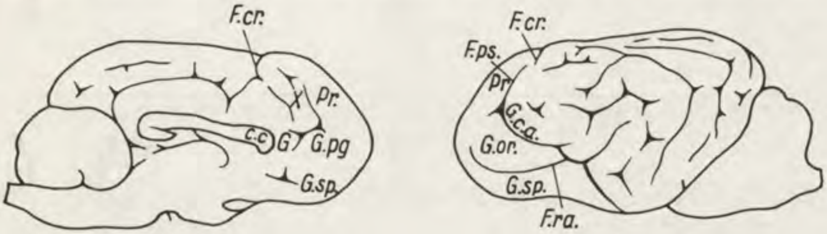

Fig. 1. Medial and lateral views of the dog brain. c.c. = corpus callosum, F. cr. = = cruciate fissure, F. ps. — presylvian sulcus, F.ra. = anterior rhinal sulcus, G. = = genual gyrus, G.c.a. = anterior composite gyrus, G.or. = orbital gyrus, G.pg = = pregenual gyrus, G.sp. = subproreal gyrus, Pr. = proreal gyrus, X = precruciate area.

Surgical procedure. Lesions were made in one stage and intended to be bilaterally symetrical. They were planned to remove the cortex as completely as possible and there was regard for avoidance of subjacent white matter damage. The anesthesia was intraperitoneally administered nembutal at 35—37 mg/kg of body weight. Following incision of the dorsal surface of the scalp, the bone superior to the frontal sinus was removed and the nasal openings were tightly packed with wax. A large defect was made in the bone overlying the prefrontal cortex. The dura was cut and retracted while the lesions were made by gentle suction with a fine aspirator. The dural edges were then sutured and the scalp closed. All lesions were made under rigid aseptic conditions. The animals received penicillin for 3 days postoperatively. Following a week's recovery from surgery, the testing was resumed and continued until the preoperative criterion was reached.

Histology. After survival of 3 months, the brains were perfused, removed and placed in formalin. Regularly spaced series of paraffin sections 20 microns thick were stained with cresyl violet and the Klüver-Barrera method to determine the extent of the lesions and thalamic degeneration. Reconstruction of the lesions (lateral and medial views) together with cross sections are shown in Figs. 2—6. A detailed description of thalamic degeneration will appear in a later report (Narkiewicz and Brutkowski, in preparation).

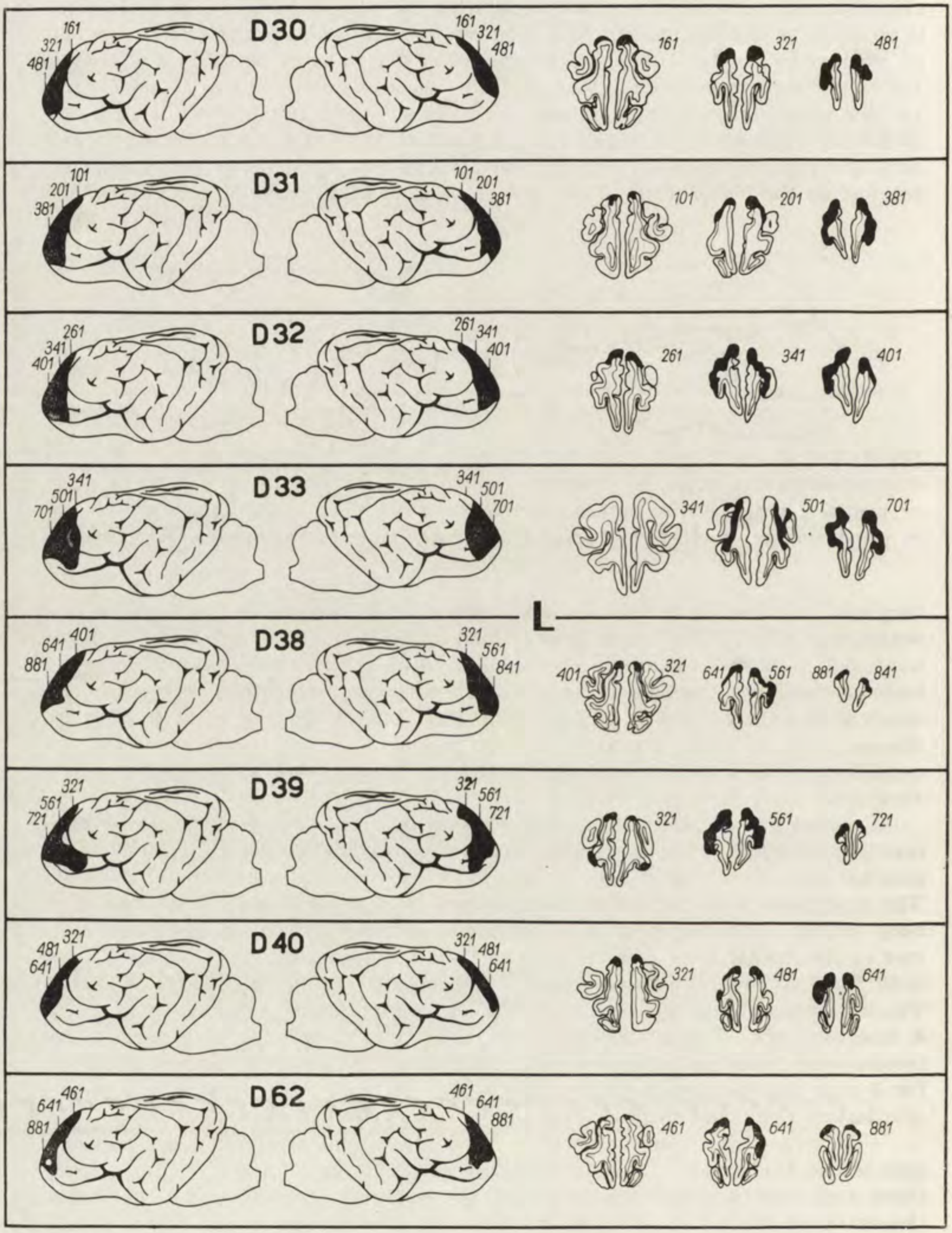
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Fig. 2.

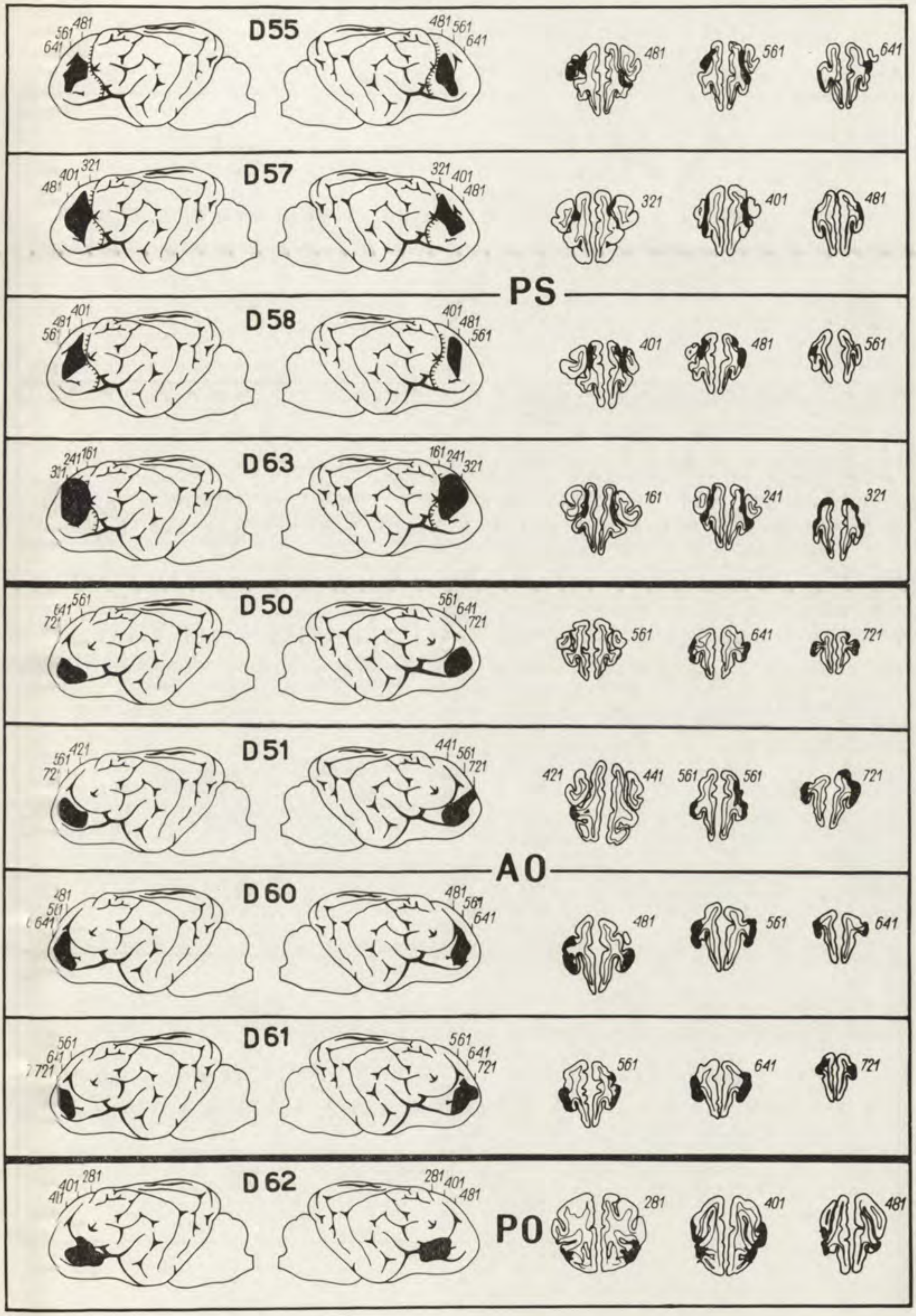
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Fig. 3.

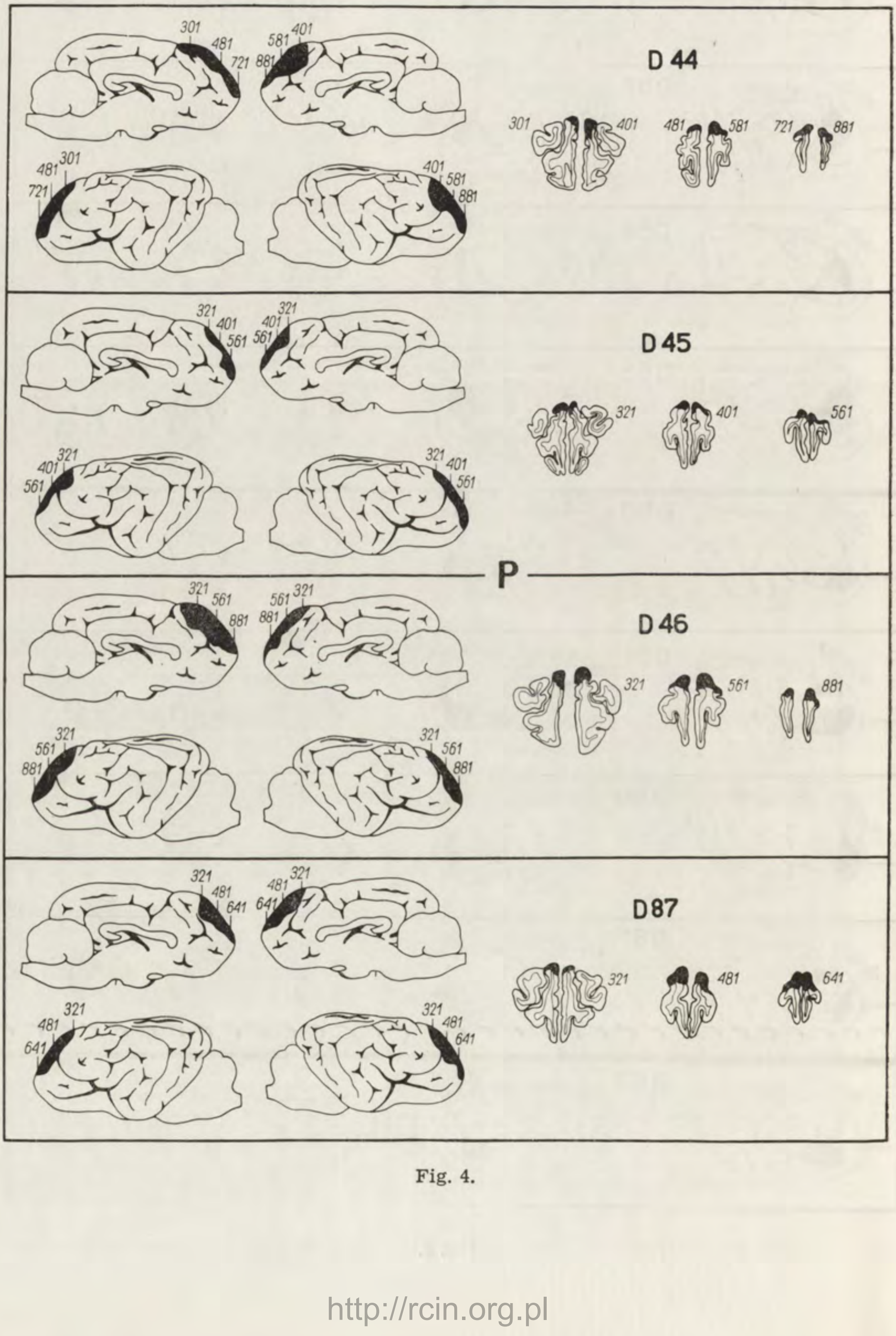
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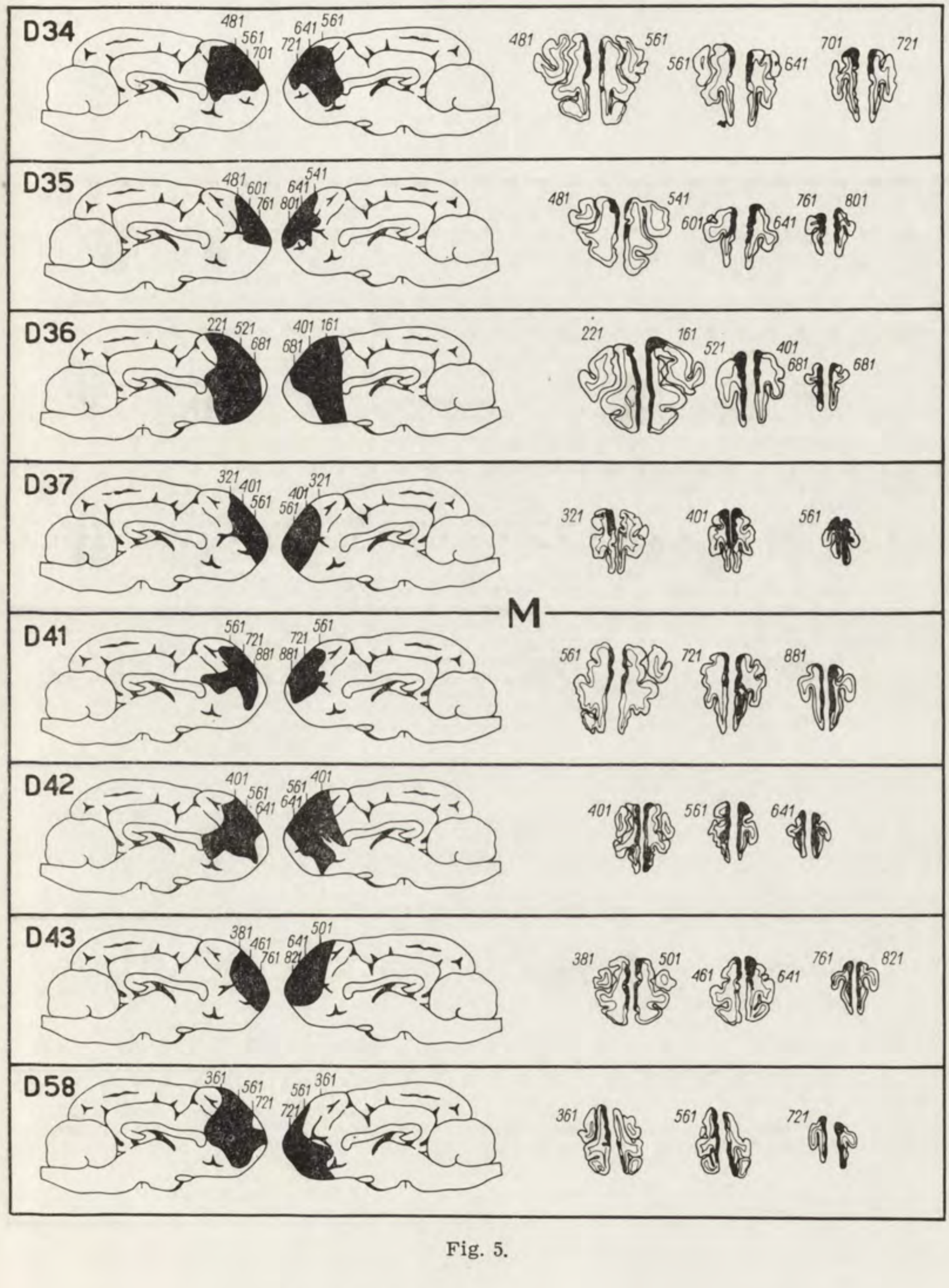
Fig. 4.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D37
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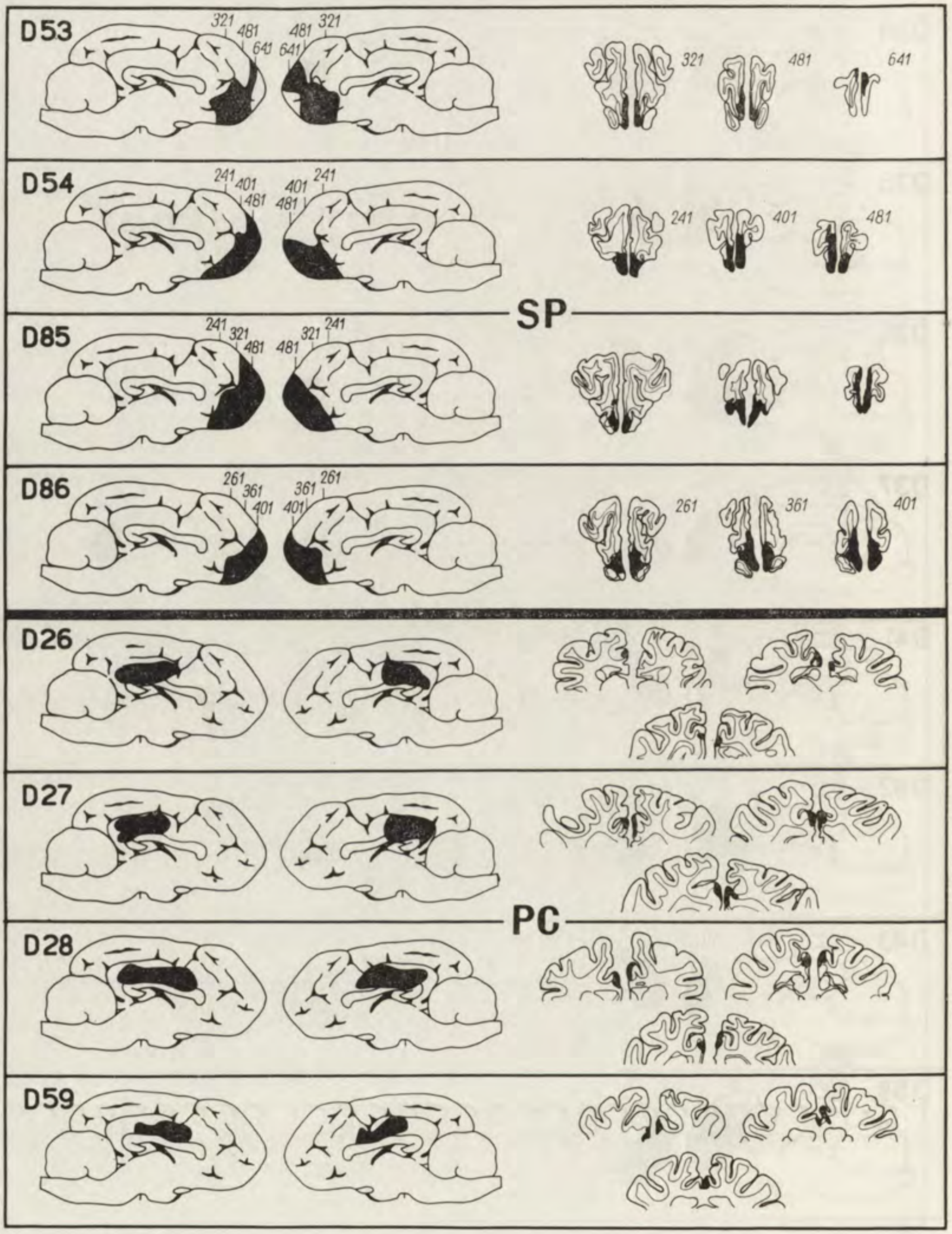
Fig. 5.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D86
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D26
D27
PC
D28
D59

Fig. 6.

RESULTS

The principal results are incorporated in Tables I—III.

CR performance on positive trials and during intertrial intervals. Postoperatively, only one animal exhibited an impairment of CR performance on positive trials. This was dog D42 with a lesion of the frontal cortex on the medial aspect of the hemisphere (Table III). The impairment was transient and probably related to the particular size of the lesion which included large portions of the precruciate and genual areas. It was found that, although the animal showed a deficit in CR performance, it responded on certain trials even at the early postoperative stages. Incidentally, it responded with the contralateral (left) forefoot, or the performance of of the trained (right) forefoot was in company with the performance of the

Table I

Total number of CR performances during intertrial intervals in the postoperative period

Dog No.	Number of CR performances
	Subgroup L15
D30	0
D31	10
D32	0
D33	0
	Subgroup L60
D38	0
D39	0
D40	12
D52	0
	Group P15
D44	4
D45	0
D46	0
D87	0
	Group AO15
D50	2
D51	0
D60	3
D61	5
	Group PO15
D62	1
	Subgroup PS15
D55	9
D57	0
	Subgroup PS60
D56	2
D63	1
	Subgroup M15
D34	47
D35	14
D36	15
D37	30
	Subgroup M60
D41	36
D42	272
D43	5
D58	12
	Group SP15
D53	0
D54	10
D85	11
D86	0

contralateral foot. Responding with the contralateral foot or stepping on the food box with both forefeet was also seen occasionally in dogs D43 and D58.

Table II

Pre- and postoperative trial and error scores, including criterion, for individual subjects trained et 15-sec. intertrial intervals

Dog No.	Preoperative			Postoperative		
	Trials (positive or inhibitory)	Errors on		Trials (positive or inhibitory)	Errors on	
		positive trials	inhibitory trials		positive trials	inhibitory trials
Lesions of the dorsolateral prefrontal cortex, subgroup L15						
D30	360	1	195	270	1	92
D31	520	1	346	270	0	64
D32	830	6	395	140	3	22
D33	200	0	120	155	0	41
Lesions of the proreal cortex, group P						
D44	345	0	252	90	0	30
D45	660	10	321	95	1	23
D46	210	0	43	90	2	17
D87	240	0	138	105	0	20
Lesions of the anteroorbital gyrus cortex, group AO15						
D50	380	6	199	115	0	20
D51	415	0	232	120	0	36
D60	225	2	122	105	0	19
D61	330	0	184	65	0	8
Lesions of the posteroorbital gyrus cortex, group PO15						
D62	345	0	204	105	0	18
Lesions of the presylvian cortex, subgroup PS15						
D55	420	0	212	70	0	14
D57	345	0	173	105	0	16
Lesions of the upper portion of the medial prefrontal cortex, subgroup M15						
D34	520	13	263	125	0	60
D35	360	3	172	115	0	32
D36	605	0	451	215	2	94
D37	280	7	143	245	2	85
Lesions of the lower portion of the medial prefrontal cortex, group SP15						
D53	510	0	228	50	0	5
D54	380	1	235	120	0	27
D85	285	0	182	75	0	10
D86	300	0	129	60	0	9
Lesions of the posterocingulate cortex, control group (PC)						
D26	420	5	291	50	3	5
D27	295	0	171	55	0	7
D28	435	0	273	50	0	3
D59	885	1	482	50	0	5

It is to be noted in Table I that the two medial subgroups showed an excess of responding during intertrial intervals (in the period immediately preceding the cortical ablation no intertrial responses were recorded in any animal). It is of interest that in spite of the failure of consistent CR performance in the initial postoperative period D42 exhibited a higher rate of intertrial responding than any other animal of these subgroups. Moreover, the excessive intertrial responding in this animal occurred both during and after the CR-depression phase. Occasionally, intense scratching of the food box was seen in this animals. These observations refute the possibility that some peripheral motor deficit incapacitated D42 to perform a consistent CR in the immediate postoperative period.

Differential inhibition. An impairment was present in all experimental groups, except groups L and PS trained at 60-sec. intertrial intervals. As may be seen in Tables II and III the two medial subgroups and the lateral subgroup trained at 15-sec. intertrial intervals showed the greatest impairment.

Table III

Pre- and postoperative trial and error scores, including criterion, for individual subjects trained at 60-sec. intertrial intervals

Dog No.	Preoperative			Postoperative		
	Trials (positive or inhibitory)	Errors on		Trials (positive or inhibitory)	Errors on	
		positive trials	inhibitory trials		positive trials	inhibitory trials
Lesions of the dorsolateral prefrontal cortex, subgroup L60						
D38	305	3	163	50	0	3
D39	135	0	75	60	0	8
D40	150	0	81	50	0	5
D52	180	2	74	50	0	4
Lesions of the presylvian cortex, subgroup PS60						
D56	580	2	270	75	5	7
D63	200	2	82	75	0	2
Lesions of the upper portion of the medial prefrontal cortex, subgroup M60						
D41	100	2	48	105	0	36
D42	170	0	63	190	66	65
D43	220	0	76	95	1	35
D58	130	0	51	105	0	43

Dog D42 who passed through an initial phase of inconsistent CR performance was the most impaired animal in subgroup M60. Early in the postoperative training, when a consistent CR performance was severely disturbed, the placings on inhibitory trials occurred sporadically. In other words, the animal showed a chaotic type of CR performance and inhibition in that he failed to respond on some positive trials and did respond on some inhibitory trials within the same testing session. When the consistent CR performance was regained, the rate of responding on inhibitory trials considerably increased.

In each instance, the impairment appeared distinct in the immediate postoperative period but declined markedly thereafter. Eventually, all animals reattained the preoperative criterion.

Similar sequelae are seen in dogs with lesions of the medial precruciate cortex (Stępień et al. 1960, 1963) and in rabbits with lesions of medial frontal cortex (Balińska et al. 1966). The animals for some days are completely unable to react instrumentally. Gradually they regain their CR performance but show a great degree of inconsistent responding and inhibition. Subsequently they display a consistent instrumental performance and a severe but temporary impairment of inhibition associated with a pronounced intertrial interval responding.

General observations. Motor behavior, tactile sensation and expression of rage. There was no measurable impairment or incoordination of gross motor ability in any animal. Dogs D34, D36, D41 and D42 were clearly hyperactive. They also screamed and barked throughout the testing session which was not the case in the preoperative period. D34 showed increased susceptibility to tactile stimuli. Dogs D34, D36 and D43 exhibited rage in the immediate postoperative period. This observation in D34 and D36 could be predicted. Brutkowski et al. (1961), and Brutkowski and Mempel (1961) reported of angry behavior in dogs with lesions that involved lower parts of the genual area. Rage behavior in D43 is not easily explicable because the genual area was spared in this animal.

Searching and gnawing behavior. All animals of groups M and SP except D41 showed evidence of pronounced sniffing licking and searching behavior. This was expressed by marked, stereotyped hyperexploratory activity at the food box and excessive licking out the food cup or sniffing within it. Dogs D36, D43, D54 and D86 kept licking far beyond the length of the intertrial interval thus postponing the presentation of the next scheduled trial.

Gnawing activity was seen in dogs D35, D37, D41, D42, D54 and D86. This consisted of occasional bites of the wooden food box of intense gnawing at the metal food cup or other objects within the animals' reach (leather harness, etc.).

These alterations in the general aspects of the pattern of behavior, which were less prominent and shorter in duration in group SP than in group M, were evidently correlated with the postoperative excess in the intertrial responding and the defect in differential inhibition. In general, they were confined to the first postoperative period and declined with the suppression of the intertrial responding and the improvement of inhibition.

It is of interest that dog D42, the one who failed to respond consistently on positive trials in the immediate postoperative period, showed the greatest degree of searching and gnawing activity.

DISCUSSION

The main results emerging from the foregoing experiment are two. First, lesions of any part of the dog's prefrontal cortex, including dorsal, lateral, basal and medial areas, disturb temporarily the retention of the inhibitory CR in a differentiation task in which the positive and inhibitory trials are separated by a 15-sec. interval. Second, lesions placed on the dorsolateral aspect of the prefrontal cortex leave the differential inhibition unimpaired when 60-sec. intertrial intervals are used. An inspection of the data reveals that animals with lesions of the upper portion of the medial prefrontal cortex (trained at both 15-sec. and 60-sec. intertrial intervals) and animals with lesions of the dorsolateral part of the prefrontal cortex (trained at 15-sec. intervals) show the greatest impairment. Accordingly, these two prefrontal lesions are considered crucial for the differential inhibition impairment. However, the demonstration that the animals with dorsolateral lesions show the impairment only when trained in the short intertrial interval schedule suggests that the deficit following dorsolateral lesions is different from that which follows medial lesions.

The finding that damage to the medial prefrontal cortex is associated with abnormal searching and sniffing activity and excessive CR responding during intertrial intervals suggests that the retention loss of differential inhibition arising from lesions of the medial prefrontal cortex reflects the release of drive functions from cortical inhibitory control. It is likely that the upper part of the medial prefrontal cortex in the dog is a major cortical area for the inhibition of drives. It should be mentioned that animals with lesions of the lower part of the medial prefrontal cortex also showed sings of increased searching at the food cup but their impairment of inhibition was inferior to that resulting from lesions of the upper part of the medial prefrontal cortex. Since lesions of the lower part of the medial prefrontal cortex were found to encroach on the upper part of the medial prefrontal cortex, it is not unlikely that the inhibitory defect in animals with lesions of the lower part of the medial prefrontal cortex is in fact a result of the damage to the upper part of the medial prefrontal cortex. This is in agreement with previous investigations concerned with conditioned-inhibition performance (Szwejkowska et al. 1965).

Animals with lesions placed on the dorsolateral surface of the prefrontal cortex (groups L, P, PS, AO and PO) display neither intertrial interval responding nor searching and sniffing activity. Since the impairment of differential inhibition in these animals occurs only in the short interval schedule, it is a reasonable hypothesis that the deficit in inhibition which follows lesions of the dorsolateral prefrontal cortex is due to excessive somatoperseverative tendencies. Previous work (Brutkowski and Dąbrowska 1965) has demonstrated that with normal animals the tendency to withhold the instrumental response on the inhibitory trial in a differentiation task is lower when CSi are presented at short intertrial intervals.

SUMMARY

The purpose of this study was to determine by the lesion method which prefrontal areas in the dog are crucial for the retention of a differentiation task. After being trained to place the forefoot on the feeder to the presentation of a positive CS and to withhold this response to the presentation of an inhibitory CS, 33 dogs were subjected to bilateral lesions in various areas of the prefrontal cortex. Four dogs received lesions of the posterior portion of the cingulate cortex, and served as controls. It was found that damage to any part of the prefrontal cortex, including dorsal, lateral, basal and medial areas disturbed temporarily the retention of the inhibitory CR when positive and inhibitory CSi were presented at 15-sec. intertrial intervals. Damage to the prefrontal areas placed on the dorsolateral aspect of the hemisphere left the inhibitory CR unimpaired when CSi were presented at 60-sec. intertrial intervals. Animals with lesions of the upper portion of the medial prefrontal cortex (trained at both 15-sec. and 60-sec. intervals) and animals with lesions of the dorsolateral part of the prefrontal cortex (trained at 15-sec. intervals) showed the greatest impairment. Thus these two prefrontal lessions were considered to be crucial for the differential ihibition impairment. Since damage to the medial prefrontal cortex was associated with abnormal searching and sniffing activity and excessive CR responding during intertrial intervals, it was suggested that the retention loss of differential inhibition arising from lesions of the medial prefrontal cortex reflected the release of drive functions from cortical inhibitory control. Animals with lesions placed on the dorsolateral surface of the prefrontal cortex displayed neither searching and sniffing activity nor

intertrial interval responding. It was hypothetized that the deficit in inhibition which followed lesions of the dorsolateral prefrontal cortex was due to excessive somatoperseverative tendencies.

We wish to thank Sabina Bielecka for testing the animals. The assistance of Janina Stefanicka in performing the histology is greatly acknowledged.

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EFFECTS OF PYRAMIDOTOMY ON INSTRUMENTAL CONDITIONED REFLEXES IN CATS. I. MANIPULATORY REFLEXES

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Owing to the renewed interest in the functions of the pyramidal and extrapyramidal pathways a certain amount of new data has been recently gathered. The effects of selective unilateral and bilateral sectioning of the pyramidal tract on motor activity were reexamined in humans (Bucy 1957), monkeys (Bucy and Keplinger 1961, Lawrence and Kuypers 1965), dogs (Gambarian et al. 1964, Górska 1966) and cats (Laursen 1966). It has been shown that many movements, even skilled, do not depend on the integrity of the pyramidal system. In agreement with these data, activation of the extrapyramidal pathways from the sensorimotor cortex after sectioning of the medullary pyramids was found to produce the same kind of movement as in intact animals (experiments on monkeys by Lewis and Brindley 1965, and on cats by Jankowska and Tarnecki 1966), and to have similar influence upon the activity of the spinal cord (Hongo and Jankowska 1967). This shows that the pyramidal and extrapyramidal pathways work in unison or mutually replace each other as was already postulated (Tower 1936, Brookhart 1952, Bucy 1957, Nyberg-Hansen and Brodal 1964, Kuypers 1964, Jankowska and Tarnecki 1966).

The aim of the present study was to make a survey of effects of pyramidotomy on various instrumental conditioned reflexes. This gave us the opportunity to study both retention and acquisition of different motor responses and to choose for our analysis the most convenient motor acts. The last point turned out to be especially important as we found that the pyramidotomy has different effects on different kinds of instrumental reflexes. The effects on manipulatory movements will be described in this paper while the effects on the instrumental reflexes derived from unconditioned reactions will be dealt with in the forthcoming paper (Górska et al. 1966)[1].

MATERIAL AND METHODS

The data to be presented were obtained from 35 cats in which pyramidal lesions were complete and in which either no damage or only partial damage of the ascending lemniscal pathways (to about one third) was found.

Three instrumental movements of the forelimb were studied: A. lifting the forelimb and placing it on a feeder (Fig. 2A), B. pressing a button fixed on a horizontal platform (Fig. 2B) and C. pushing a button fixed on a vertical wall (Fig. 2C).

The movements had to be performed with right limbs. They were reinforced with food given in a feeder, which could be turned automatically by pressing or pushing a button by the animal, or else by the experimenter. All the reflexes were established without any sporadic conditioned stimuli, i.e. to the experimental situation. The instrumental movements differed in respect to their complexity. Placing the limb on a feeder was a very simple movement, a mere flexion. It was established by reinforcing spontaneous movements of scratching around the bowl when the animal expected food. Pressing or pushing the button required aiming the paw in the direction of a semicircular (pressing) or circular (pushing) screen encompassing a button, inserting the paw inside the screen, and then pressing or pushing the button respectively with adequate strength. The diameter of the screen was of 30 mm, just enough for a paw to be put inside. In order to establish these reflexes, at the beginning of the training period the food was given inside the screen. The accidental button pressing, accompanying attempts to reach the food with the right paw, were then automatically reinforced by turning a feeder which offered another portion of meat. After a number of such repetitions, the animals started to put their right paws inside the screen and press or push the button without any provocation. This was followed by turning the head in the direction of the feeder and awaiting a reward from it.

The training of all the reflexes was continued for about 20 experimental sessions (with 20 movements per session) beginning from the moment when the instrumental movements first appeared. At the time of the operation, the learnt movements were performed at a constant rate and in a fairly uniform way. After pyramidotomy the experiments were resumed in about a week, and the state of the reflexes was tested once or twice a week for 2 months (at least 10 sessions with 20 trials per session). When the reflexes had to be retrained in the postoperative period similar techniques were used as in original training.

The pyramids were sectioned at the level of the trapezoid body through a hole in the base of the skull. The extent of the lesions was always checked histologically. The brains were fixed in 4% formalin and embedded in paraffin. Serial sections were cut at the level of the lesion and 2—3 mm above and below it, in order to analyze both the lesion and the descending (pyramids) and ascending (medial lemniscus) degeneration (Fig. 1). The sections were stained alternately with hematoxiline-eosine and Klüver-Barrera method.

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[1] A preliminary note has been already published (Górska et al. 1965).

RESULTS

A. Placing a leg on the feeder. Eight cats were trained to put the right forelimb on the feeder. After both the unilateral (in 4 cats) and the bilateral (in the remaining 4 cats) pyramidotomy, the trained reflexes

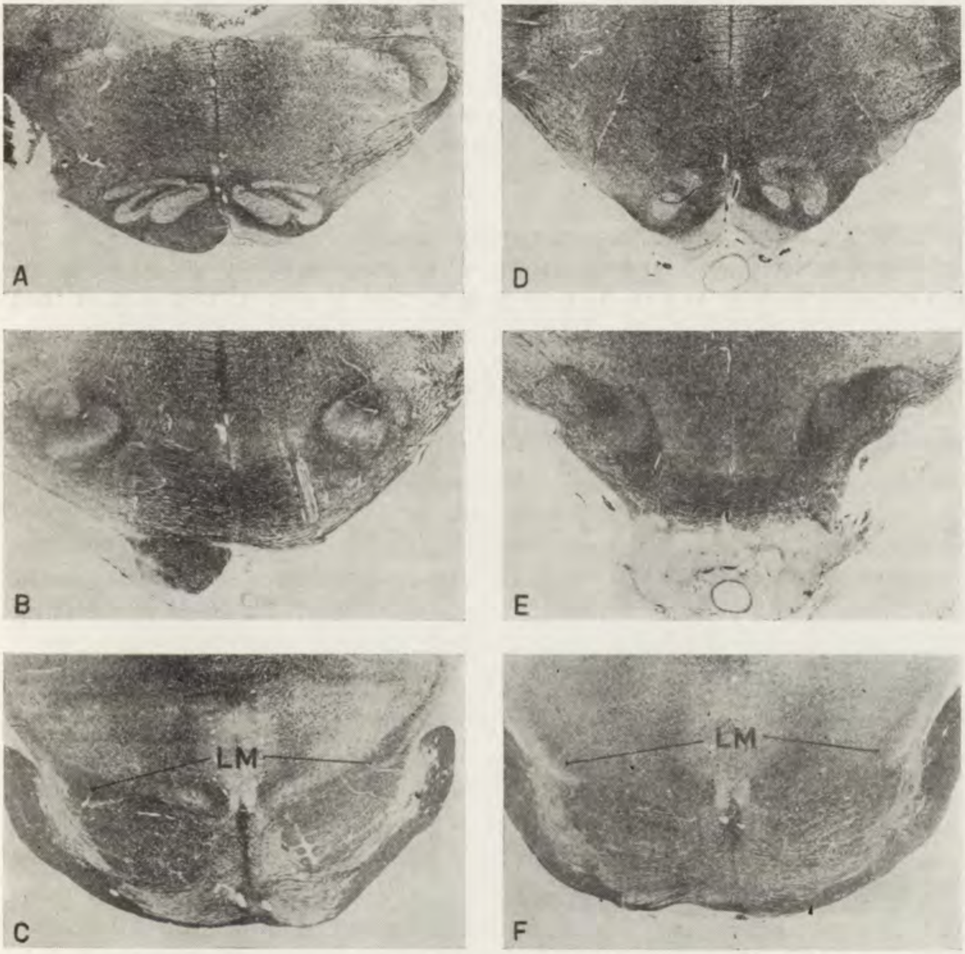

Fig. 1. Photographs of transverse sections of the medulla and pons in 2 cats after a unilateral (A—C) and a bilateral (D—F) pyramidotomy. Paraffin sections, stained with Klüver-Barrera method. A and D show a complete degeneration of pyramids at the level of the inferior olive. The corresponding maximal extent of the lesion at the level of the pyramidal section is shown in B and E. The resulting degenerations of the medial lemniscus can be seen in C and F. In C a comparison of the surface occupied by the lemniscal fibres on the intact and lesioned side reveals that not more than 1/5—1/4 were damaged on the latter side. In F a similar number of lemniscal fibres seems to be degenerated.

were preserved. The animals started to put the right limb on the feeder as soon as they found themselves in front of it. The only difference in their behaviour, in comparison with the preoperative period, was that after placing the limb on the feeder they did not withdraw it as they used to do previously. As this prevented the execution of the next movement, a supplementary piece of meat was placed on the floor of the cage after the cat had finished eating. This helped the cat to assume the correct starting position. Fig. 3A shows that when the latter procedure was used the frequency of movements, did not change significantly, except for the first two experimental sessions when it dropped to 60—70% of the control preoperative values.

In another group of 9 cats (5 after a uni- and 4 after a bilateral pyramidotomy), the same reflex was trained in the postoperative period. All the cats learned it and both the final results and the rate of acquisition of the reflex were similar as in intact cats. The only difference was that they did not withdraw the limb from the feeder as was the case with the cats trained before the operation.

B. Pressing a button. The effects of pyramidotomy on button-pressing were tested in 7 cats. Before the operation, pressing the button was automatically followed by turning a bowl. As there was a deterioration of the reflex after pyramidotomy, during the first 5 testing sessions even the most primitive movements, if only directed to the button were reinforced by having the bowl turned by the experimenter. Beginning with the 6th session, however, the full movements were required for getting the reinforcement.

On the whole, 3 kinds of reaction were present: 1) a successful pressing with a single movement, 2)pressing after a few unsuccessful attempts (in which the cat failed to put the leg into the screen or the strength of pressing was not sufficient), and 3) aiming the limb at the screen and placing it near the opening, with or without attempts to put the limb inside. The right hand diagram in Fig. 3B shows percentages of these three categories of responses before and after the unilateral (in 4 cats) and bilateral (in 3 cats) pyramidotomy. In both groups, there is a deterioration, which is somehow stronger in the bilaterally operated animals. It is worth noticing, however, that even during the first five sessions the correct movements appeared. The improvement in the unilateral cats occurred fairly quickly. The bilaterally pyramidotomized cats required an additional training (between the 5th and the 6th testing sessions) during which they had practiced putting the limb into the opening of the screen. This was done by offering the cats some food within the screen as during the preliminary training. After such retraining, they

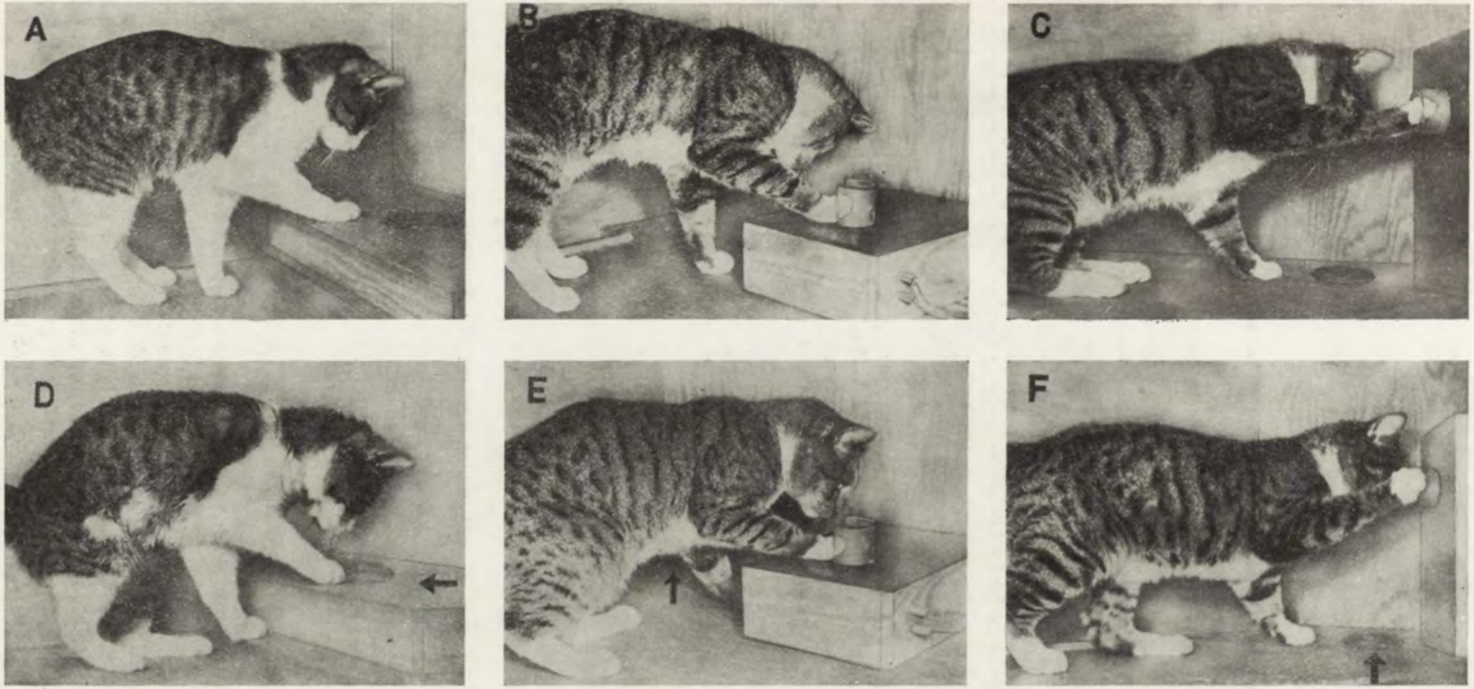

Fig. 2. Examples of placing a limb on a feeder (A, D), pressing (B, E), and pushing a button (C, F). Upper rowbefore operation. Lower row— after a bilateral pyramidotomy. The after operation photographs were taken at the end of the testing period in A—C and after retraining in D—F. Arrows mark the place from which food was given.

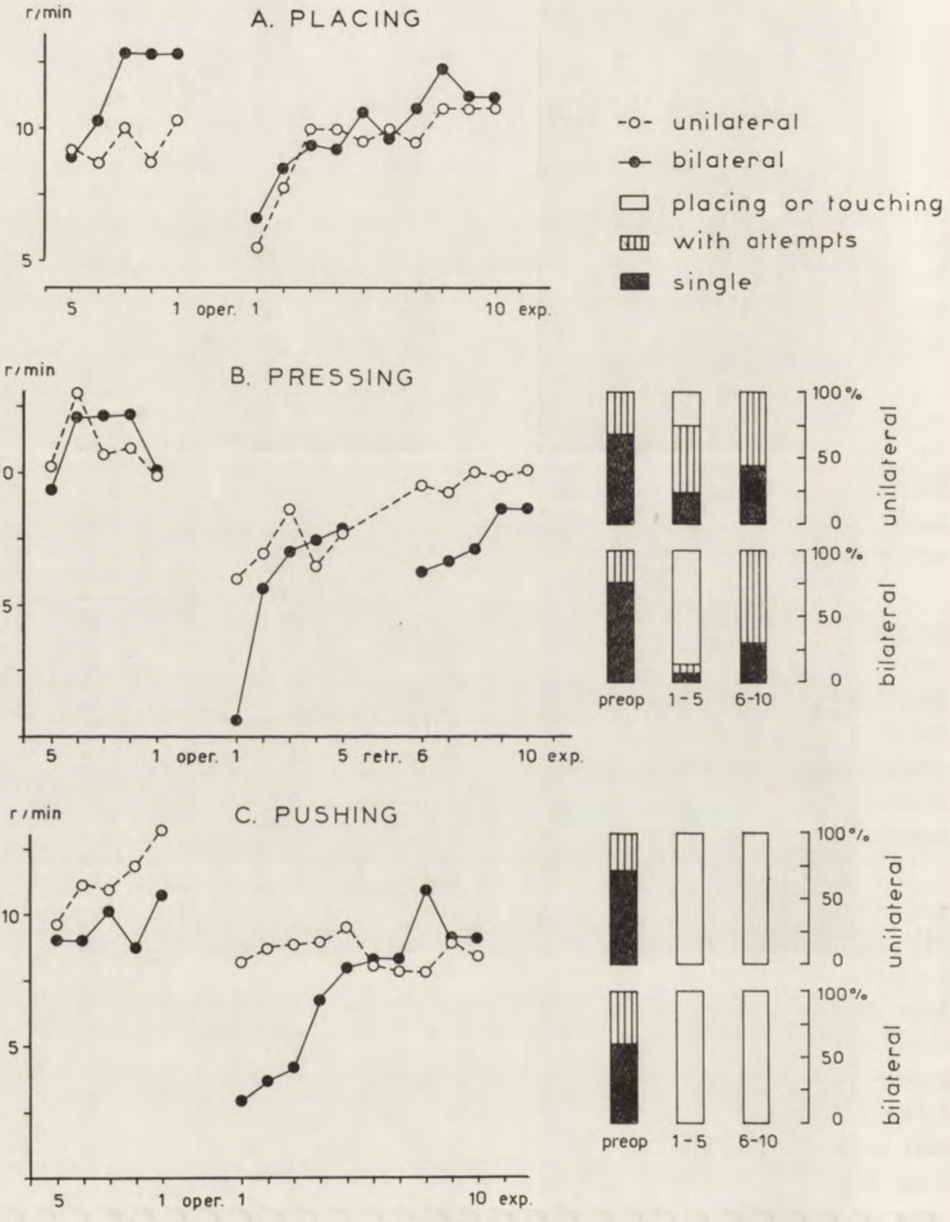

Fig. 3. Effects of pyramidotomy on frequency and proportion of different kinds of movement in placing, pressing and pushing instrumental reflexes. The curves show average frequencies of instrumental movements (for 20 trials) in two groups of unilaterally and bilaterally pyramidotomized cats, during the last experimental sessions before and the first testing sessions after the operation. The right hand diagrams in B and C give the percentages of different kinds of instrumental movements (see text). The data are for the 5 last preoperative sessions, and from 1 to 5 and 6 to 10 postoperative testing sessions.

were able to press the button in 100% of trials, although, most often, only after one or few unsuccessful attempts.

The frequencies with which reflex appeared before and after pyramidotomy are plotted in the curve in Fig. 3B. The decrease in frequencies during 6 to 10 postoperative sessions might be due to the increased number of unsuccessful attempts preceding the final movements. During the first 5 testing sessions, however, this decrease seems independent of the preceding factor, since usually the very first movements were reinforced.

In another group of seven cats (3 after a unilateral and 4 after a bilateral pyramidotomy), an attempt was made to establish the reflex of pressing the button in the postoperative period. This proved to be possible, although with some difficulties. The cats were rather awkward in putting the proper limb within the screen and needed some practice to improve their skill.

Similar difficulties were observed in the case when the cats had to reach a piece of meat from a small groove. They were able to do it but usually only after several unsuccessful attempts, consisting of scratching the walls of the groove.

Because of the difficulties in getting inside the screen, the unilaterally pyramidotomized cats prefered to use the ipsilateral instead of the limb contralateral to the lesion. Therefore movements of the former had to be prevented (Jankowska and Górska 1960). During the proper training (without food on the button), some cats lost their interest in the task when too many attempts remained unsuccessful and without any reward. In these cats (one uni- and 3 bilaterally pyramidotomized), the screen encircling the button was removed so that they pressed the bare button.

The final achievements of the cats trained after the operation were analogous to those seen in the cats trained before and tested after the pyramidotomy. There was a greater proportion of pressing movements preceded by unsuccessful attempts than in intact cats. But again it must be stressed that all the cats proved to be able to acquire the highest precision of performance, although only in some percentage of movements.

C. Pushing a button. The next test-reflex resembled, in many respects, the button-pressing, except for the fact that it required aiming the limb at a different direction and that the final movement was pushing instead of pressing (Fig. 2C). It was more difficult, as judged from a slower rate of the preliminary training and a greater number of unsuccessful attempts preceding final pushing (Fig. 3C).

The effects of pyramidotomy on the reflex of pushing a button were analyzed in 8 cats (4 after a unilateral and 4 after a bilateral lesion). In all the animals, the reflex was preserved although its last element was missing. The cats lifted the forelimb and aimed it at the button, as before the pyramidotomy, but without inserting the limb inside the screen and pushing the button. 2 uni- and 2 bilaterally operated cats touched the screen and sometimes an attempt was made to get inside. The remaining animals merely approached the screen or touched the wall on which it was fixed. During the first 5 testing sessions, all these movements were reinforced. After that time several attempts were made to reestablish the reflex in its preoperative form. It turned out, however, that the cats were unable to insert the limb into the tube even when a piece of meat was put inside, and they did not correct those movements which were not reinforced.

In such a situation, the proper retraining or a postoperative training was impossible, and, as there was no spontaneous improvement during the whole postoperative period (over 3 months), the deficit in the quality of performed movements was considered to be permanent (see right hand diagram in Fig. 3C).

The frequency of movements appearing in the postoperative period, however, was not much smaller in comparison with the movements before pyramidotomy (Fig. 3C) except in the 3 first sessions in the bilateral cats.

DISCUSSION

On the whole, our results are in agreement with the data (Bucy 1957, Bucy and Keplinger 1961, Górska 1966, Lawrence and Kuypers 1965, Laursen 1966), showing that the pyramids are not necessarily involved in "voluntary" movements.

All the instrumental reflexes described in this paper were present after pyramidotomy and might appear with similar regularity as before the pyramidal section. The main impairment was in the skill with which the movements were performed.

The simplest movement of placing the forelimb on the feeder was fully preserved although without taking down the limb and reassuming the starting possition. So was the first and the second component of the button-pressing and button-pushing reflex, i.e. the flexion of the limb up to the level of the button. The second component of these reflexes — aiming the limb at the screen surrounding the button was also preserved. The last component of the button pressing appeared to be just within the possibilities of the cats after pyramidotomy; they had difficulties in inserting their paws in the small opening of the screen and in the majority of cases succeeded only after a few attempts. In several cases, the task was so difficult that the cats resigned from attempting it, and either the degree of difficulties had to be diminished (by removing the screen encircling the button) or the special training of putting the limb inside the screen had to be carried out. Failing to put the paw inside the screen seems to be caused either by the animals not sufficiently adducting their digits, or else because they failed to insert the limb directly over the hole.

In the case of the reflex of the button-pushing its last element was practically lost. The best what the animals succeeded to do was to touch the screen from outside or inside, but without the proper movement of pushing. Similar deficit was found in the reaction from which the instrumental reflex was derived: the cats were unable to reach the food from the narrow horizontal tube. The nature of both these deficits would need special analysis and further experiments. They might be due to a not quite correct aiming of the limb or to an insufficient coordination of the movements. It is quite possible, however, that it is a „pushing" itself which requires a special pyramidal control, or a pushing when holding the limb lifted in the horizontal position. One of the symptoms of the pyramidal damage in humans is that they can not hold their arms stretched out. If the latter hypothesis were true, the loss of „pushing" could not be explained by an impairment in activity of the distal muscles, which was postulated to be the main impairment after pyramidotomy (Lawrence and Kuypers 1965), but it might be due just as well to the deficit in the proximal motility.

SUMMARY

The effects of a unilateral and bilateral section of medullary pyramids were studied on 3 manipulatory instrumental reflexes: placing a limb on a feeder, pressing a horizontal button and pushing a vertical button. The first reflex was well preserved after pyramidotomy. In the second reflex, there was an impairment in inserting the limb inside the screen encircling the button, and the cats pressed it usually only after a few unsuccessful movements. Both these reflexes might be established postoperatively in naive cats. The button-pushing reflex was preserved partially (without inserting the limb into the opening of the horizontal screen and the very pushing). In all the reflexes, there was only a transient decrease in their frequencies. The main impairment of the reflexes was that of the coordination and the skill of the movements.

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EFFECTS OF PYRAMIDOTOMY ON INSTRUMENTAL CONDITIONED REFLEXES IN CATS. II. REFLEXES DERIVED FROM UNCONDITIONED REACTIONS

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After sectioning of the medullary pyramids, cats (Górska et al. 1966), similarly to monkeys (Bucy and Keplinger 1961, Lawrence and Kuypers 1965) are able to perform various movements belonging to the category of manipulatory instrumental reflexes. In the present paper it will be shown that, on the contrary, pyramidotomy may almost completely abolish the instrumental conditioned reflexes derived from certain unconditioned reactions like scratching (Thorndike 1911, Fedorov 1955, Jankowska 1959) and cleaning or licking of the skin (Thorndike 1911, Górska et al. 1961). The latter group of instrumental reflexes was found to have some particular properties, if compared with lever-pressing, box-opening and other aimed manipulatory movements. The main pecularity is that they start to appear in a form very similar to that of the unconditioned reaction but afterwards they become extremely simplified and reduced to only some elements of the original reaction. In spite of this the instrumental reflexes derived from unconditioned reactions do not seem to differ essentially from other instrumental conditioned reflexes. They might even be considered as the simplest models of the complex learnt movements. (Jankowska, unpubl. Doctor's thesis 1962, Konorski 1962, Górska, unpubl. Doctor's thesis 1965).

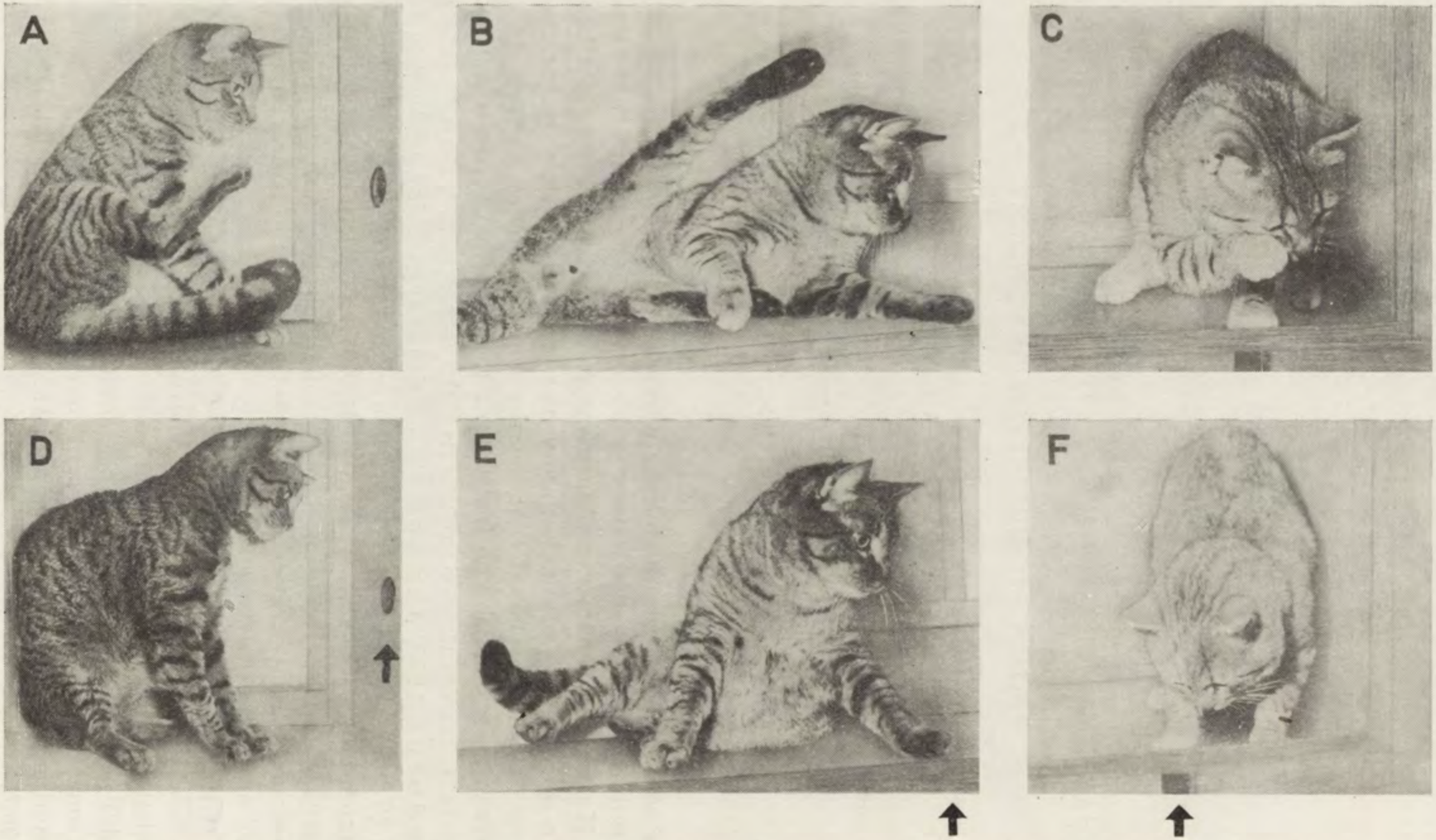

Fig. 1. Examples of scratch (A, D), cleaning (B, E), and rubbing (C, F) instrumental reflexes. The photographs in the upper and in the lower row were taken before and after the bilateral pyramidotomy respectively. Arrows mark the place from which food was given.

METERIAL AND METHODS

Three instrumental reflexes derived from the scratch movements with the hindlimb, cleaning the anal region accompanied with the lifting of the hindlimb, and the rubbing of the skin over the head with the forelimb, were used as the test responses. As it was already described (Jankowska 1959, Górska et al. 1961) the easiest way of establishing such instrumental reflexes is to evoke the required unconditioned reactions and reinforce them whenever they appear in the experimental situation. After a number of repetitions, stimulation of their receptive fields becomes unnecessary and the required reactions start to appear as conditioned movements. The scratch, cleaning and rubbing reactions were originally evoked by putting a cotton wool into the ear, moistening the skin around the anus, or over the cheek, respectively. When the reactions were difficult to evoke, either glue was used instead of water for moistening the skin or a clip was attached to it.

In the process of „instrumentalization" the above reactions became more and more simplified. In its final preoperative form the instrumental „scratch reflex" consisted in the cat sitting down and lifting the hindlimb (with an adduction and a slight flexion in all the joints), usually without touching the skin and with its head turned in the direction from which food was given (see Fig. 1A, D). Sometimes, a few rhythmic components were also present. The instrumental cleaning reflex appeared in a form somewhat similar to the scratch reflex. When well established, it consisted in the cat sitting on one side and lifting the opposite hindlimb (with a slight abduction in the hip joint), the head being directed to the place from which food was expected (Fig. 1B, E). The instrumental rubbing reflex consisted in the cat lifting its forelimb and bringing it either close to, or in contact with its cheek (Fig. 1C, F). All the movements had to be performed with the right limbs. They were reinforced with food (a piece of meat given by the experimenter) and trained without any sporadic conditioned stimuli to the experimental situation.

The effects of pyramidotomy on retention or acquisition of the instrumental scratch, cleaning or rubbing reflexes were studied in the same cats in which the manipulatory movements were analyzed (Górska et al. 1966). Usually, in each cat one to three different instrumental movements were trained before, and one or two others after a pyramidotomy. The movements were trained in different experimental situations and were never confused by the animals (Wyrwicka 1958).

The general procedure was similar to that described before, with 20 preoperative sessions (20 movements per session) since the establishment of the reflexes and 1—2 testing sessions a week after the pyramidotomy. When the reflexes were lost, testing was discontinued after 5 sessions (about 6 weeks, 10—30 min. per session) and retraining was started. During the retraining and the postoperative training of new reflexes similar techniques were used as in intact animals.

RESULTS

A. The scratch reflex. Out of 12 cats (6 after the unilateral and 6 after the bilateral pyramidotomy) a very pronounced deterioration of the reflex was found, both in respect to the quality of movements and their frequency, in 3 uni- and 2 bilateral cats. In the remaining 3 uni- and 4 bilateral cats an almost complete loss of the reflex was found.

The right hand diagram in Fig. 2A shows the animals' performance in the pre- and postoperative period. In the unilaterally pyramidotomized cats the number of high and moderate responses was reduced and the number of the small responses increased. Moreover, a great deal of the movements which appeared were of much smaller amplitude than any movement before the operation and should be classified as very small or even dubious. In the bilaterally pyramidotomized cats almost all the movements were of the latter category and only 11 % might be classified as small responses. After the first 5 testing sessions an attempt was made to improve the deteriorated reflexes or to reestablish the lost ones. During the retraining in every second session some cotton was put into the ear of the animal in order to evoke the unconditioned scratch reaction or at least facilitate the instrumental movements; under such conditions the very small or dubious movements were never reinforced. During the alternating testing sessions the ratios of different kinds of movement was found to be improved, although far below the preoperative period.

In Fig. 2A the frequencies of the first two categories of movement (high and small, but undubious) were plotted for unilateral and bilateral cats separately. After the operation, there was a marked decrease in the frequency of instrumental reflexes. During the retraining (only data for testing sessions, without any facilitation by a cotton wool ear plug, were plotted), there was a gradual but very slow increase in the frequencies of trained movements which parallelled the improvement in their quality.

In another group of 9 cats, attempts were made to establish the instrumental scratch reflex in a postoperative period. In intact cats it can be achieved in 3—5 days. Out of 5 unilaterally pyramidotomized cats, in one animal the instrumental movements appeared between the 10th and 20th session, in 3 cats between the 20th and 30th session, and in the last one, there was no effect within 30 sessions. Out of 4 bilaterally pyramidotomized cats, only in one did some rudimentary instrumental movements appear between the 20th and 30th session, and in the other 3 cats, any instrumental reactions were lacking within 30 sessions. When the reflexes were present, the frequencies of movements were low: below 3.5 and 0.5 movements/min. in unilateral and bilateral cats, respectively.

It should be noted that pyramidotomy affected not only conditioned scratch reflex but also the unconditioned reflex itself. Fig. 3 shows the average frequencies of the unconditioned scratching which appeared within 5 minutes with the cotton wool ear plug before and after the bilateral pyramidotomy. These frequencies were systematically lower after sectioning the pyramids. Similar results were found in unilaterally operated cats, although the decrease of frequencies was less pronounced than after the bilateral pyramidotomy.

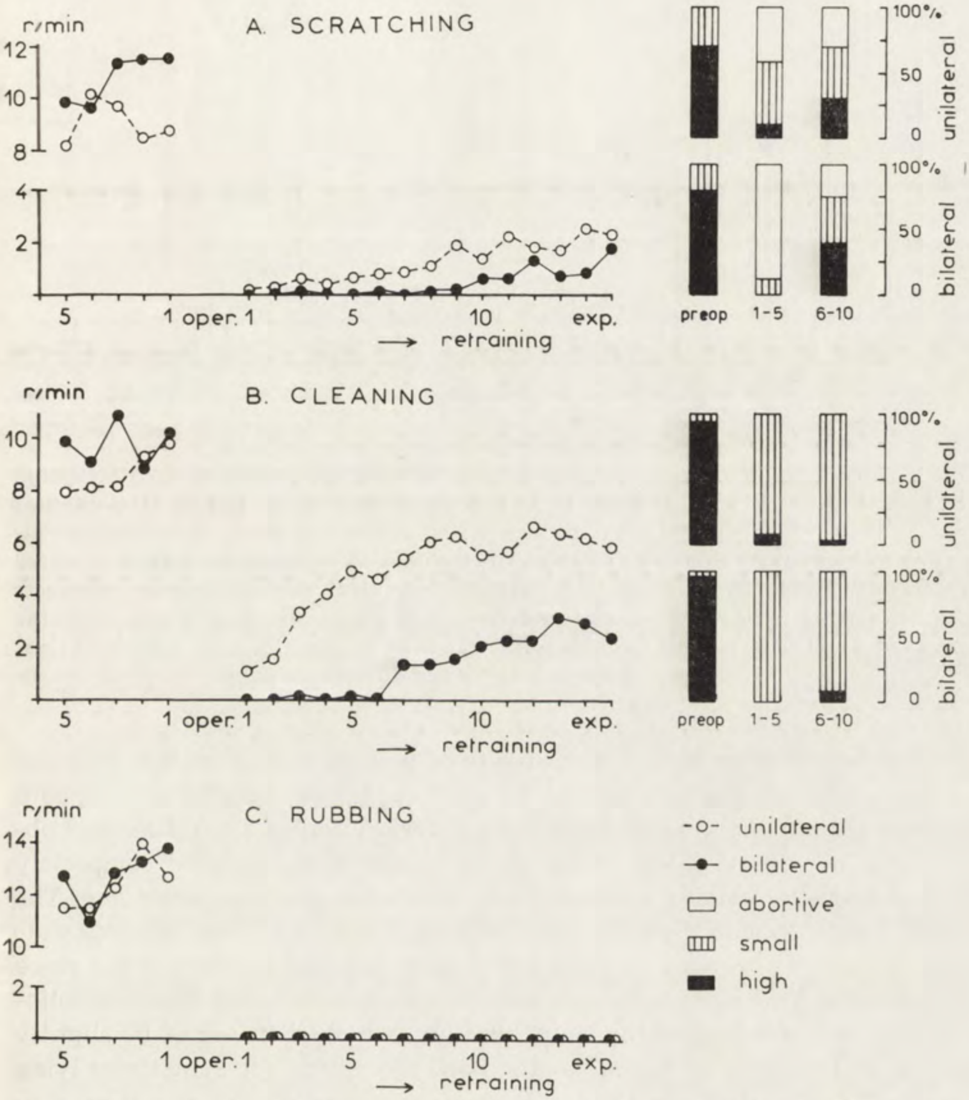

Fig. 2. Effects of pyramidotomy on frequency of the instrumental reactions and on proportions of different kinds of movements in scratch and cleaning instrumental reflexes. The curves give the average frequencies for 20 trials (in 2 groups of unilaterally and bilaterally pyramidotomized cats) during the last experimental sessions before, the first 5 testing sessions after the pyramidotomy and the next 10 testing sessions during the retraining (see methods). The right hand diagrams in A and B give the percentages of the different kinds of movement during the last preoperative and from 1 to 5 and 6 to 10 postoperative testing sessions.

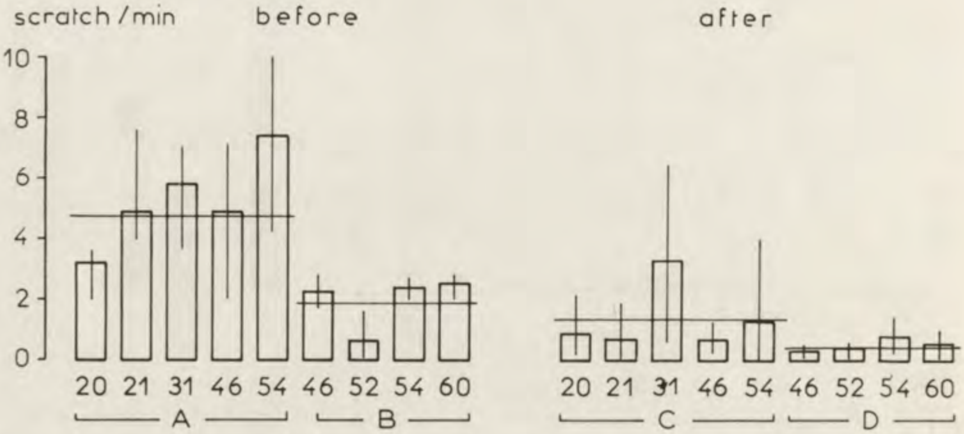

Fig. 3. Frequency of scratch reactions during the 5 minute period of the stimulation of the ear (see text) in the bilaterally pyramidotomized cats. A and C, data obtained during the preoperative training and the postoperative retraining of the instrumental scratch reflexes. B and D, reactions in the cats in which scratching was tested independently of any training. The data for individual cats are average numbers from 5 testing periods of 5 minutes, a few days before and 3—6 weeks after the pyramidotomy. The vertical lines show the range of frequencies. The horizontal lines give the average values for the different groups.

B. The cleaning reflex. The effects of pyramidotomy on the cleaning reflex were tested in 5 unilaterally and 6 bilaterally operated cats. In both groups of animals, a very pronounced deterioration of the reflex was observed. The high isolated lifting of the hindlimb disappeared completely and the only remaining component of the reflex was a postural one. The typical behaviour in the postoperative period was as follows: the cats walked around the cage, as they did previously, and just in front of the place from which food was given they sat down on the left side; this was followed by an unloading of the right hindlimb which then might be slightly lifted. In unilaterally operated cats, both the sitting (or sometimes lying on the floor) and lifting the limb were more pronounced and more frequent than in the bilateral cats and showed a spontaneous improvement. After 5 testing sessions in which all the reactions resembling the movements in the preoperative period were reinforced, retraining was started. During this retraining, the receptive field of the unconditioned reaction of cleaning, i.e. the anal region, was stimulated in every second session in order to evoke the required movements of the hindlimb. It was found that moistening the skin, which was used in intact animals was almost uneffective in evoking the reaction after pyramidotomy. Therefore some stronger stimuli like glue or attaching a clip to the skin were utilized.

During the alternating testing sessions an improvement of the instrumental reflexes of lifting the limb was observed in both the unilateral and bilateral cats (in the latter, however, only in 3 out of 6 animals). During the retraining, the amplitude of movements of the hindlimb was somewhat increased, although they remained unisolated, being the elements of postural synergies as before the retraining. Because of the unclear character of the small movements, it was rather difficult to differentiate more categories than of just small (among which some might be dubious movements) and high movements, which were much smaller than before the operation (Fig. 2B).

In the three bilaterally pyramidotomized cats in which the retraining was uneffective, not only the movements of the hindlimb but also the reaction of sitting down was missing.

In another group of 4 cats (3 with a unilateral pyramidotomy and 1 with a bilateral one), a postoperative training of the instrumental cleaning reflex was carried out. The limited number of animals trained postoperatively was due to the fact that in the rest of the animals tested (2 with a unilateral lesion and 6 with a bilateral lesion) the unconditioned cleaning reflex could not be regularly evoked, even when using a much stronger stimulation than in normal animals. In 3 cats with a unilateral lesion in which the unconditioned reflex was present, the instrumental cleaning reflex could be established. The instrumental movements appeared somewhat later than in normal animals (on average, after 3.7 sessions as compared with 2.2 in intact ones). Their frequency and amplitude was as low as in pyramidotomized cats trained before the operation, and the most pronounced was their postural component. In one cat trained after a bilateral pyramidotomy the instrumental cleaning reflex could not be established within 20 sessions.

C. The rubbing reflex. Out of 11 cats trained before operation, 5 were subjected to a unilateral and 6 to a bilateral pyramidotomy. In all the operated cats the instrumental rubbing movements practically disappeared. The animals performed only very small flexions with the trained limb whose character was not clear. They did not resemble the movements from before the pyramidotomy and might be confused with stretching the trained limb toward the hole in the floor, through which the food was usually given. The attempts to retrain the reflex also proved to be unsuccessful. When the strong stimulation of the skin on the head was used the animals performed distinct rubbing reactions during the sessions in which the unconditioned stimulation was applied. When it was lacking they continued to perform only the small dubious movements as before the retraining.

In another group of cats (5 with a unilateral lesion, and 3 with a bilateral one), a postoperative training of the instrumental rubbing reflex was carried out. While in intact animals the instrumental responses usually appeared after 2—3 sessions, in none of the pyramidotomized animals did any distinct instrumental movements appear within 15—20 experimental sessions.

DISCUSSION

Sectioning of pyramids affected the instrumental scratch, cleaning and rubbing reflexes in a similar way. The trained movements, if present, appeared usually in an abortive form and with very low frequencies. The retraining, even 3—5 times longer than the original training, only partially reestablished the scratch and cleaning reflexes and was uneffective in the case of the rubbing reflex. In the instrumental scratch reflex, the retraining improved the quality of movements rather than their fequency, while in the instrumental cleaning reflex the movements remained small or abortive but their frequency increased. Similar final results were obtained in cats in which the scratch and cleaning reflexes were trained only after the pyramidotomy.

These results show a serious divergance between the effects of the pyramidotomy on the presently analyzed reflexes and on the manipulatory instrumental movements described earlier (Górska et al. 1966), the latter being relatively well preserved. The difference is even more striking as the two groups of reflexes were tested in the same animals; a cat might perform, for example, almost perfect movements of pressing a button while it was unable to do more than a few abortive flexions of the hindlimb instead of the instrumental scratch movements, or it made a high flexion of the forelimb, lifting it up to the level of the button to be pushed, but was unable to make a similar flexion and touch its own head.

The explanation of such divergence might be searched in the different effects of the pyramidotomy on the original reactions from which the instrumental reflexes were derived. The reaction of stretching the forelimb in order to reach the food, being at the basis of all the manipulatory movements studied (placing the limb on the feeder and pressing or pushing the button), was well preserved after the pyramidotomy. There were some deficits in this reaction if the task was more difficult, requiring special coordination of movements, e.g. when the opening, in which the food was left, was very small. Similar deficits appeared in the respective instrumental movements.

As to the effects of pyramidotomy on the unconditioned scrath, cleaning and rubbing reactions, their deterioration was of a different kind. If present, they appeared in the complete form, but their threshold was raised in all the three cases. When using the same stimulation as in intact cats the scratching and rubbing reactions appeared with much lower frequencies, and the cleaning reflex practically did not appear. A stronger stimulation of the skin in the case of rubbing and cleaning reactions evoked the former fairly easily and with a high frequency; the latter might appear, but usually with low frequencies.

The raised thresholds of the unconditioned reactions might be explained by a removal of a pyramidal facilitation of the transmission in spinal reflex paths (Lundberg and Voorhoeve 1962, Lundberg 1964). In their turn, the rise in thresholds might be at the basis of the deterioration of the respective instrumental reflex. The last point should be commented on. In an analysis of mechanisms of the instrumental reflexes derived from the unconditioned reactions we postulated (Jankowska, unpubl. Doctor's thesis 1962; Górska, unpubl. Doctor's thesis 1965) that the unconditioned reflex arcs of the latter are utilized in evoking the instrumental movements and that the new conditioned connections being once established, these reflex arcs can be activated form some cortical or subcortical structures involved in the instrumental conditioning. If so the loss of the scratch, cleaning and rubbing reflexes might be caused by two factors: elimination of the descending volleys (voluntary impulses) in the pyramidal fibres and/or loss of the pyramidal facilitation in the required reflex paths. The first factor is probably less essential than the second one, since some instrumental movements appeared both in the case of the scratch and cleaning reflexes and the section of pyramids did not prevent the manipulatory instrumental movements to be performed. On the other hand, the raised thresholds would explain the smaller efficiency of descending volleys in the extrapyramidal paths and the resulting decreased frequency, of movements and their smaller amplitude. In the case of the purely spinal scrath reflex lowering the strength of cutaneous stimulation similarly decrease the amplitude of the scrath beats as well as their frequency (Sherrington 1906).

The three instrumental reflexes derived from scratch, cleaning and rubbing reactions were affected to a different degree. The instrumental scratch reflex might be relatively less impaired because of its wide receptive field and a possibility that the pyramidal fibres leaving the pyramids above the level of their sectioning (Kuypers 1958, 1960), might facilitate some of its reflex paths.

In the cleaning reflex the proper movements were very small, especially in the bilaterally pyramidotomized cats, but might be partially improved if only the animals learned to assume the correct position. This position was not always identical with a position preparatory for cleaning the anal region. It might be just as well sitting down, or lying on one side with the bending of the whole body and unloading the right hindlimb. It seems quite possible that in this case the lack of the pyramidal facilitations might be counterbalanced by facilitations within the postural synergies.

In the case of the instrumental rubbing reflex, there seems to be no direct correlation between its deterioration, or rather loss, and with an increase in the threshold of the unconditioned reaction. This point will be analyzed in the forthcoming paper (Górska, in preparation). In this place, we would only point out that the effects of the pyramidotomy (removal of the pyramidal facilitation) might be enhanced by an inhibition from an antagonistic reflex of stretching the forelimb for food. In the present experiments, the experimental situation was rather unfavorable for the appearance of the instrumental rubbing reflex as the reinforcement was given through a hole on the level of the floor and the animals had a very strong tendency both to lower their head and to stretch their forelimb in the direction of the hole, instead of lifting it and trying to touch the cheek. This postulated antagonism between the direct alimentary reaction and the instrumental rubbing movements was not seen before the pyramidotomy, probably because the tendency to perform the latter was much stronger when the reflex was properly facilitated by the pyramids.

In analogy with scratch, cleaning and rubbing reactions we can assume that the reflex of stretching a limb in order to reach food also needs some pyramidal facilitation. After section of the pyramids at the medullary level, the latter might be supplied, however, by fibres leaving pyramidal tract above the level of transection, thus preserving the reflex.

The described effects of pyramidotomy were rather unexpected and might seem paradoxical, as the comparatively simple conditioned reactions like in the instrumental scratch, cleaning and rubbing reflexes were much more affected than the skilled and precise movements. They could be, however, understood in view of the double role of the pyramidal system: a general facilitatory, gate-like opening (classified as tonic by Tower 1935, 1940) and a more specific, assuring skill and coordination of movements (called phasic by Tower 1940). The first one being fundamental, its lack can explain the disappearance of the instrumental reflexes devoid of pyramidal facilitation.

SUMMARY

The instrumental conditioned reflexes derived from the unconditioned scratch, cleaning the anal region, and rubbing the cheek reactions were seriously impaired by the pyramidotomy. In the case of the first two reflexes, their frequency was much reduced and the required movements of the hind limbs appeared in an abortive form or had very small amplitudes. The retraining improved the reflexes only partially. The postoperative training was effective only in some cases, and the rate of establishment of the reflexes was slower than in intact animals. The instrumental rubbing reflex was completely abolished by the pyramidotomy and could not be retrained. The postoperative training of this reflex was found to be uneffective. In all the animals, there was found an increase in thresholds of the unconditioned scratch, cleaning and rubbing reactions. This increase was assumed to be due to the lack of the facilitatory pyramidal influences and to be the main cause of the deterioration of the respective instrumental reflexes.

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EEG AND BEHAVIOR REACTIONS UPON STIMULATION OF NONSPECIFIC THALAMIC NUCLEI IN UNANESTHETIZED CATS

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It has long been demonstrated that 6 to 12 shocks per second delivered to the ,,nonspecific" thalamic reticular system (NTS) produce recruiting responses, RRs (Dempsey and Morison 1942, Morison and Dempsey 1942, Hanbery and Jasper 1953). Knowledge of these observations is largely derived from acute experiments (cf. Jasper 1960, Narikashvili 1962, Buser 1964). More recently, attention has been focused upon the stimulation of NTS in chronic experiments. Evarts and Magoun (1957) recorded RRs in freely moving cats and found no signs of alterations in gross behavior pattern. Acoustic stimulation reduced the RRs. However, this reducing effect faded with repeated stimulation. Also, electrical stimulation of the brainstem reticular formation resulted in a reduction of the RRs but this was abolished when pentobarbital was administered. Yamaguchi et al. (1964) have shown that stimulation at a frequency of 8 to 10 per second and 1 msec. duration is the most satisfactory condition for the RRs. If 4 stimuli are delivered each second, the recruiting activity is small and inconsistent. On the other hand, at a frequency of 15/sec. the EEG increases and the animal is awake. Generally, the form, latency and duration of the RR potentials in unanesthetized cats are similar to those recorded in acute experiments (Yamaguchi et al. 1964, Sakhiulina and Merzhanova 1965). Sakhiulina and Merzhanova (1965) discovered that the pattern of the RR activity is different in different points of the same cortical region. Yama-

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[1] In the early phase of this research, the authors worked with R. P. Kashakashvili.

guchi et al. (1963) showed that the RRs were clear-cut in the sleeping animal, although, at the paradoxical stage of the sleep, they could be hardly elicited, and if they occurred they were poorly pronounced. Angyan et al. (1964) found that the RRs tended to diminish when recorded in the cat placed in the situation in which a conditioned reflex had been trained previously. It is now evident that the RRs can be recorded in both freely moving dogs (Sakhiulina and Merzhanova 1964) and wake humans under neurosurgical conditions (Housepian and Purpura 1963). Stimulation of the reticular nucleus at a frequency of 10 per second in man results in widespread activity of the recruiting type. On the other hand, high-frequency stimulation in a sleeping person leads to a decrease of the EEG amplitude and alertness in the behavior.

We have succeeded in confirming and extending some of the above-mentioned observations. Knowledge of how the NTS functions in intact animals tested under chronic conditions bears on the analysis of brain activity, particularly that revealed in cortical inhibition.

METHOD

Seven cats were used in this study. These were implanted chronically with electrodes in various portions of the brain, both cortically and subcortically. Stimulating electrodes were implanted in the centromedian nucleus and the reticular nucleus of the NTS. Surface recording electrodes were placed on the somatosensory, auditory cortex and the suprasylvian gyrus. Depth recording electrodes were oriented in the midbrain reticular formation. The recording electrode in the somatosensory and auditory areas was placed in the region, giving the best pronounced evoked response. Silver wire 0.3 mm in diameter was used for cortical recordings. The electrode tips consisted of small bare balls. Burr hollows were placed into the skull to reach the lamina vitrea. Electrodes were implanted by inserting the electrode balls into the hollows. The electrodes were fixed to the calvarium with stiracrylic plastic, their free ends being soldered to a radio valve plug which was attached to the calvarium also by means of stiracrylic plastic. Glass-insulated steel wire, 0.1 mm in diameter, was used for the depth electrodes. These were implanted pair-wise in subcortical sites (distance between electrode tips was approximately 1.0—1.5 mm). The stereotaxic coordinates for the sites of electrode placement were determined, using the atlas by Jasper and Ajmone-Marsan (1954). The depth electrodes were introduced into the brain with the Horsley-Clark stereotaxic instrument. They were fixed to the skull with the stiracrylic plastic an soldered to a radio valve plug (socket).

Electrical stimulation of the NTS was produced by a square pulse generator through a radio frequent unit, with the output resistance measured 400 ohms, and with an isolation unit. The stimulus threshold increased considerably with time, presumably due to the growth of the glial and connective tissues around the electrode tips. Hence, the stimulus values given are relative. Cortical recording was bilateral (the electrode tips were 10 mm apart) and monopolar (the „indifferent" electrode was placed in the bone overlying the frontal sinus). The electrical activity was recorded on an Alvar electroencephalograph and on a Cossor cathod ray oscillograph.

Experiments were carried out in a screened sound-proofed room. The animals were placed in a small grounded cage and observed throughout the entire experimental session. In the present investigation, the records were obtained on three cats: An, Ban and Gan.

RESULTS

When the cat was drowsy or asleep the amplitude of the RR potentials built up to attain its maximum after 4—7 shocks (Fig. 1A, C). On the other hand, if shocks were delivered continuously the potentials proceeded to wax and wane with bursts occurring every 2.5—4.0 sec. The activity seen in Fig. 1B is remarkably similar to the alpha rhythm in man. Upon the stimulation of the centromedian nucleus the RRs were more clearly pronounced in the somatosensory area than in any other cortical areas (Fig. 1A). During wakefulness, the amplitude of the potentials built up on the first shocks. After attaining their maximal level the potentials began to wane. They then followed the stimulation rhythm with no signs of bursts and, subsequently, they continued to wane (Fig. 8). The „waning" stage appeared to drag on. A similar observation was made when shocks were delivered at a relatively high fraquency under barbiturate narcosis (Narikashvili 1962). In intact animals, this type of RR activity is more frequent than the „classical" type, characterized by spindle patterns. Strong stimulation induced the maximal RR activity which showed no tendency to diminish (Fig. 2). In some instances, the „increasing" stage tended to persist. For example, during an experimental session it consistently lasted 7—12 seconds, that is, the amplitude of the potentials attained its maximum after 50—100 shocks. In such cases, the animal was awake prior to stimulation. During stimulation, the amplitude of the potentials increased. Fig. 5C shows that a clear-cut increase coincides with the animal's closing the eyes.

Shocks delivered to the centromedian nucleus usually produce diphasic potentials in the somatosensory cortex: a small positive potential is followed by a large negative one (Fig. 1D and 2G). On the other hand, the potential recorded from the suprasylvian cortex is negative (Fig. 1D). However, as shown in Fig. 2D the potential in the somatosensory cortex may be also negative, sometimes. Note that during the early stage of stimulation the shape and amplitude of the potentials show marked variations due to the interference with the background activity. In the course of later trains of stimuli, the background activity declines and the character of the potentials (+, −) becomes stabilized. Reversing the direction of stimulation results in the occurrence of purely negative potentials. The latency of the negative potential is about 20 msec. (Fig. 2D). The positive deflection seen in the remaining oscillograms is elicited after a latency of about 13

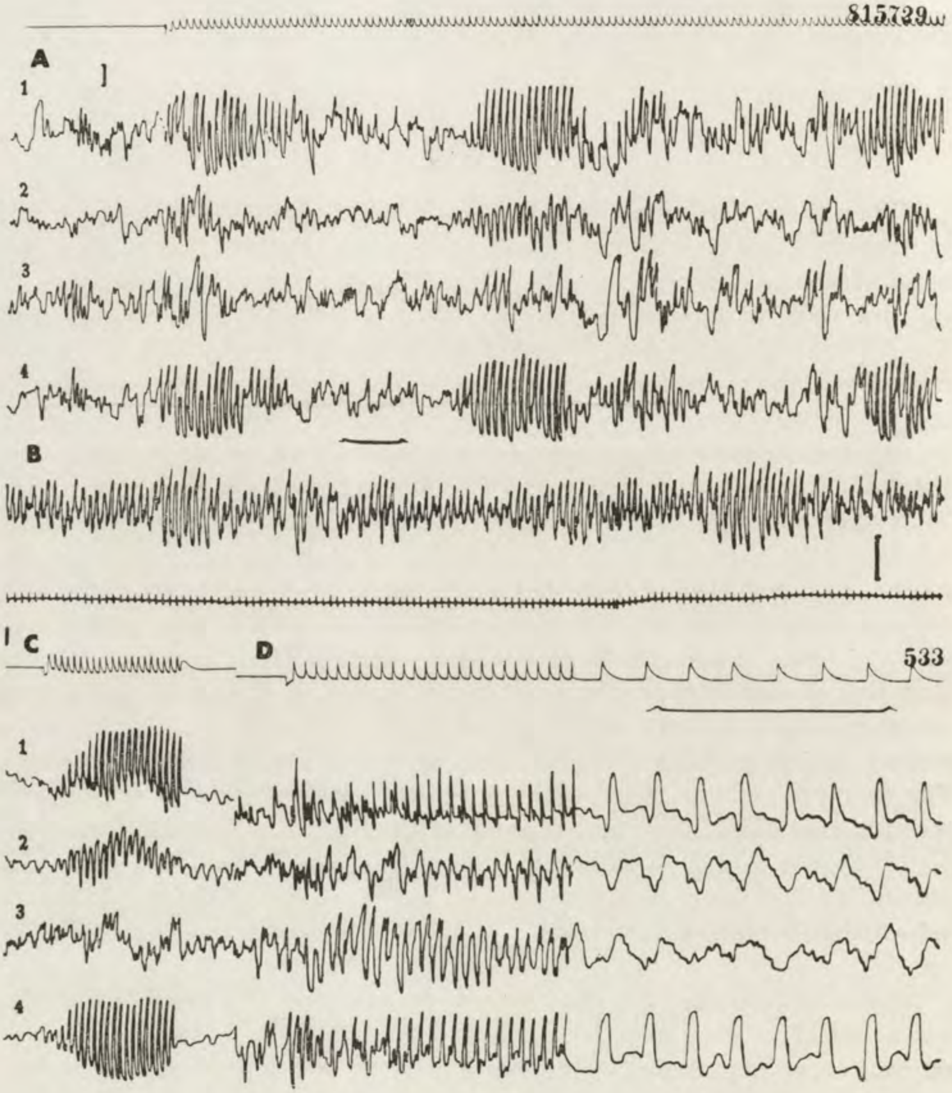

Fig. 1. Recruiting response (RR) in normal cats

A, C and D, cat "Ban" with chronically implanted electrodes. Stimulating electrodes, left centromedian nucleus (NCM). Recording: 1, left somatosensory area; 2, left acoustic area; 3, left suprasylvian gyrus; 4, right somatosensory area. Bipolar recording. Date: December 10, 1964. The cat is asleep. A, RRs following stimulation at a rate of 8/sec. (0.2 msec., 25 v.); C, same type of stimulation as in A except that the voltage increased to 40 v. D, date: December 16, 1964; the cat is drowsy, the shocks are delivered at a rate of 6/sec. (0.2 msec., 50 v.), a slow speed of the paper is followed by a rapid one. B, cat "An" with chronically implanted electrodes. Stimulating electrodes, left centromedian nucleus (NCM). Recording electrodes: 1, left suprasylvian gyrus; 2, left ectosylvian gyrus. Date: December 12, 1963. The cat is asleep. RRs obtained from stimulation at a frequency of 8/sec. (0.5 msec., 15 v.). In no instance, there was seen an alteration of the behavior pattern. Time: 1 sec. Calibration in A, C and D: 25 microvolts, in B: 100 microvolts. Stimulus artefact indicated in all records.

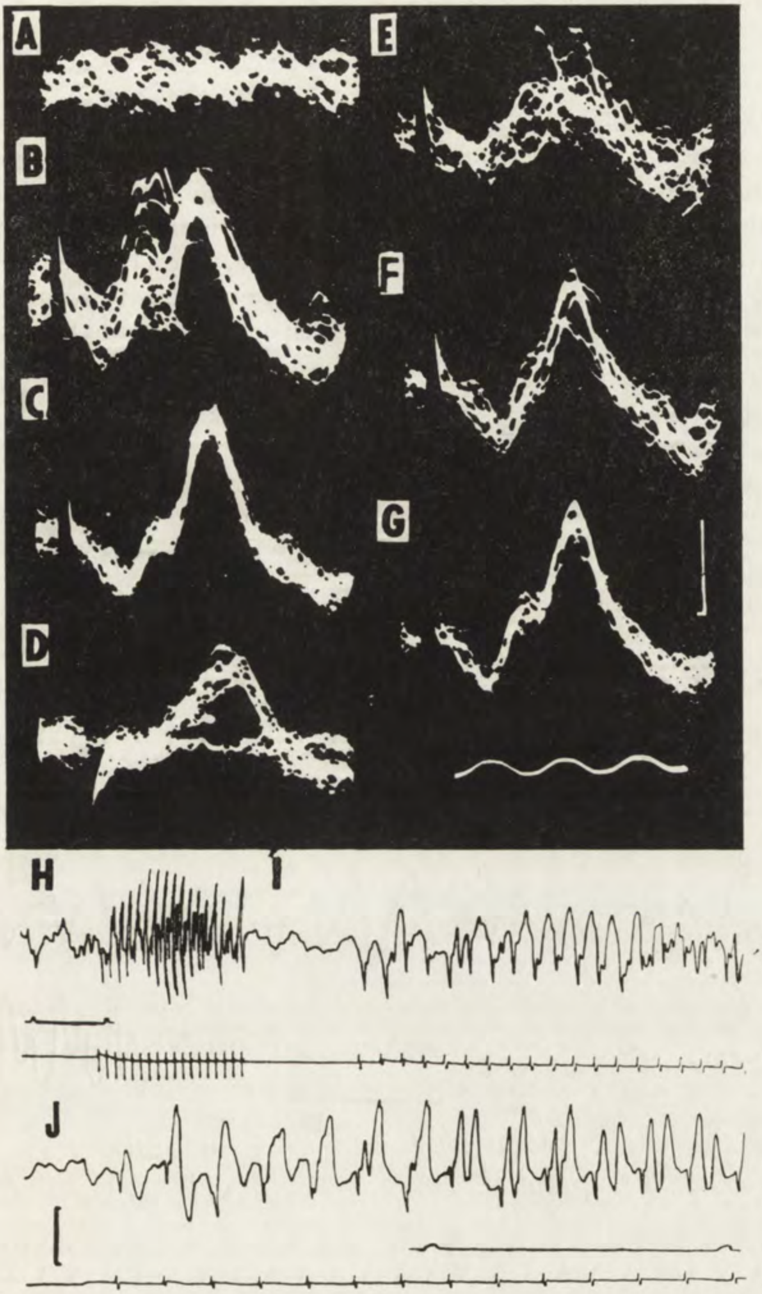

Fig. 2. RRs as a function of the intensity and frequency of stimulation of the centromedian nucleus

A, cat "Ban". Date: May 5, 1965. Recording electrodes, homolateral somatosensory area. Unilateral recording. Stimulus triggered sweep. A, background activity, ca. 20 flashes. B, early stage of stimulation (7/sec., 0.2 msec., 50 v.); C, stimulation continued for a few seconds. D, reversed direction of stimulation, early stage of stimulation. E, 30 v.: F, 40 v.; G, 50 v. Records taken approximately 1 sec. after the onset of stimulation. The cat was asleep. Time: 20 msec. Calibration: 100 microvolts in G. H—J, cat "An". Date: December 12, 1963. Recording electrodes, parietal area. H, stimulation rate 9/sec. (10 v., 0.5 msec.); I, 13/sec.; J, 6.5/sec. The cat was asleep. Time: 1 sec. Calibration: 100 microvolts.

msec. After a delay, this positive wave is followed by the negative wave. As shown by Jasper (1960), the origin of the positive wave is different from that of the negative wave. The records in the right portion of Fig. 2 show the RR potentials induced by stimulating the NTS at varying intensities; recording the activity was started 2 sec. after the delivery of the shocks. Note variation of potential shape for low-intensity stimulation and a stereotyped pattern of potentials for high-intensity stimulation.

It is known that RRs depend on the stimulation frequency. In Fig. 2, records from a sleeping animal are shown under conditions of varying stimulation frequency. The optimal frequency for a typical RR activity was 9 shocks per second (Fig. 2H). When the frequency was 6 per second the first 7 shocks elicited unstabilized potentials, and the subsequent shocks were associated with the occurrence of a double negative potential (Fig. 2J). When the frequency was 10 per second a burst activity was considerably smaller than under conditions of 8/sec. frequency (Fig. 2I). It is a common observation that stimulation of the NTS does not produce a diffuse cortical activation. This observation was made also in unanesthetized animals. As pointed out previously, it was found that evoked potentials

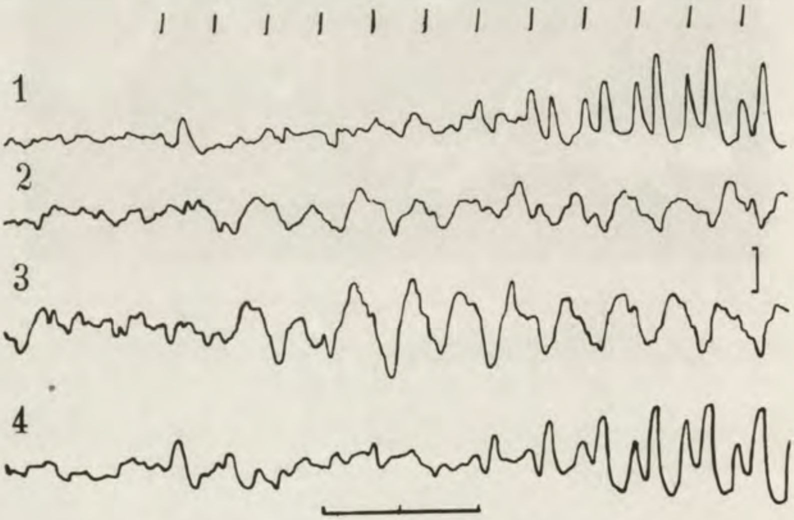

Fig. 3. Cortical „Irradiation" of slow wave activity

Cat "Ban". Date: December 16, 1964. Recording electrodes: 1, right somatosensory area; 2, left acoustic area; 3, left suprasylvian gyrus; 4, left somatosensory area. Stimulation of the centromedian nucleus. The cat is asleep. The record shows the electrical activity of the cerebral cortex at the early stage of stimulation (6/sec., 30 v., 0.2 msec.). Time: 0.5 sec. Calibration: 50 microvolts.

were different when recorded from different cortical regions. Furthermore, they at first could be recorded from the parieto-temporal region, and after 1 sec. also from the somatosensory region (Fig. 3), whereby giving an impression of a widespread cortical „irradiation". Moreover, the increasing RR phases within different cortical areas did not necessarily coincide, which was also noticed under acute conditions (Narikashvili 1958). Thus, it was found that in one cortical area the increasing RR phase persisted for more than 1 sec., whereas in another area an unstabilized small-amplitude discharge pattern occurred, or a decreasing response in one region was associated with an increasing response in another region. This suggests reciprocal interrelations between the cortical regions. Finally, the spread RRs in the cortex of unanesthetized animals was found to depend on the functional state of the brain rather than on the intensity of

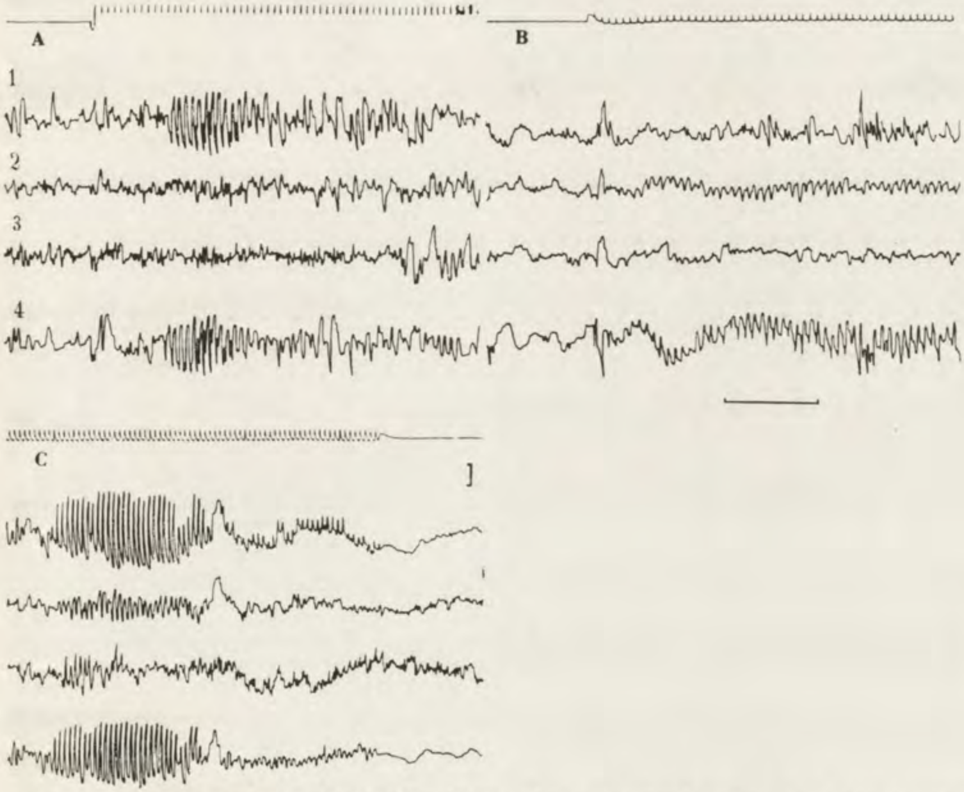

Fig. 4. Variation of the electrical activity of the cerebral cortex as a consequence of the stimulation of the nonspecific thalamic nucleus.

Cat "Ban". Same placement of the stimulating and recording electrodes as in Fig. 3. A, date: December 10, 1964; B, date: December 11, 1964; C, date: December 9, 1964. Stimulation strength: 27 v. (0.2msec.). C, stimulation rate 9/sec.; A and B, stimulation rate 7/sec.

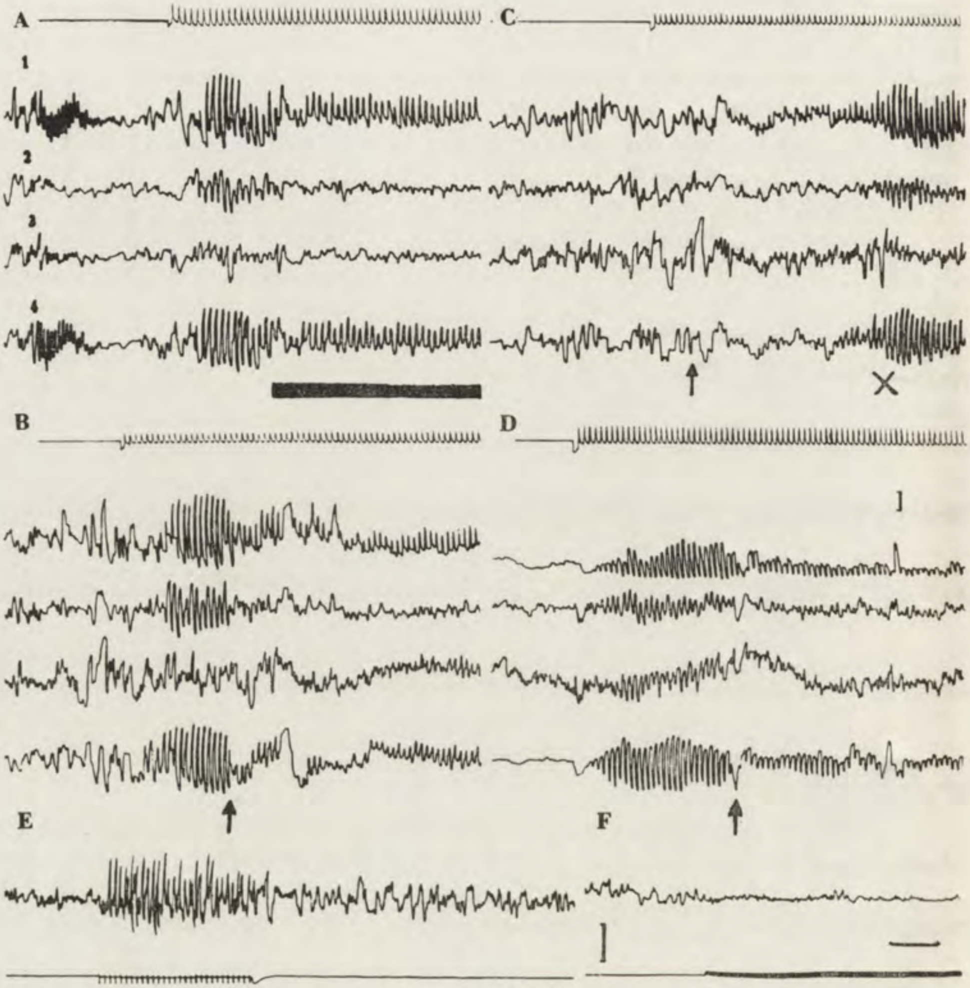

Fig. 5. Depression of the RR following external stimulation. The effect on RR activity of high-frequency stimulation of the centromedian nucleus.

A, cat "Ban". Date: December 11, 1964. Same placement of stimulating and recording electrodes as in Fig. 1A. A, the cat is asleep; the discharge on the left as a spontaneous one. Stimulation of the centromedian nucleus (8.5/sec., 0.2 msec., 30 v.) elicited RR activity. In response to the presentation of an acoustic stimulus of 50 cy/sec. (indicated), the cat reacted with its ears. B, same conditions as previously. At the indicated place the cat was called to and it awoke. C, immediately after the onset of the stimulation the cat was called to (arrow) and it awoke; with continued stimulation the cat began to fall asleep (at the upward arrow the cat closes its eyes). D, the cat slept; stimulation of the centromedian nucleus produced RR activity; at the upward arrow the cat opened its eyes "voluntarily". E and F, cat "An". Date: December 12, 1963. Same placement of stimulating and recording electrodes as in Fig. 1B. E, the cat was drowsy. Stimulation of the centromedian nucleus (8/sec., 0.5 msec., 10 v.) produced no behavioral response. F, stimulation at a rate of 100/sec. awoke the cat. Time: 1 sec. Calibration: 25 microvolts in D, and 100 microvolts in F.

stimulation of the NTS. Thus it was shown that in three successive experimental sessions the RR activity pattern markedly varied over the cortex despite isogeneous stimulation and sleep conditions: on the first day, the activity occurred only in the somatosensory region; on the second day, it was recorded from the homolateral somatosensory and auditory regions; and, finally, on the third day, it was seen in all three regions studied (Fig. 4). This observation suggests that the distribution of the RRs is determined by the functional, continuously varying factors rather than by structural, stable ones.

Both the RRs and ,,spontaneous" bursts (Fig. 5A), recorded in the sleeping animal, often displayed the same distribution over the cortex. Our data have failed to reveal whether the ,,spontaneous" activity determines the evoked activity that varies from one cortical region to another, or the tendency to ,,spontaneous" reproducing the pattern of the evoked activity occurs as a result of the stimulation applied repeatedly to the NTS. With low-frequency stimulation, e.g. 6/sec. (Fig. 2J), two waves sometimes followed each electrical shock. On the other hand, when stimuli of great intensity are used, he RRs are recorded from widespread cortical regions, the rhythm of the evoked potentials being entirely determined by the rhythm of the stimulation. Moreover, the ,,spontaneous" bursts then fail to occur and the background electrical activity is reduced. This indicates that, under these conditions, the electrical activity of the cortex is largely influenced by the activity of the stimulated NTS (Fig. 2). As mentioned above, the RRs may be confined to some cortical regions only, e.g. to the somatosensory and auditory regions of both hemispheres, or to the somatosensory and auditory regions of the stimulated side. All attempts (an increased duration or repeated stimulation) to produce a widespread cortical activity from the stimulation of the centromedian nucleus were unsuccessful. However, when the stimulation is amplified the RRs usually occur also in other cortical regions.

When the stimulation with a strength sufficient to produce the RRs in the somatosensory regions persisted for many minutes, the RRs failed to occur outside the recording regions, whereas inside the recording regions the RR bursts ceased to occur and the diminished potentials followed the frequency of the stimulation. Under such conditions, ,,spontaneous" bursts were also seen only in somatosensory regions. It is likely that this was due to long stimulation. A similar phenomenon was observed in acute experiments (Terzian et al. 1952).

We confirmed the finding showing that the RR activity varies as an animal goes from a drowsy to an activated state, and vice versa. In the waking state the RRs were found to be poorer (increased latent period and

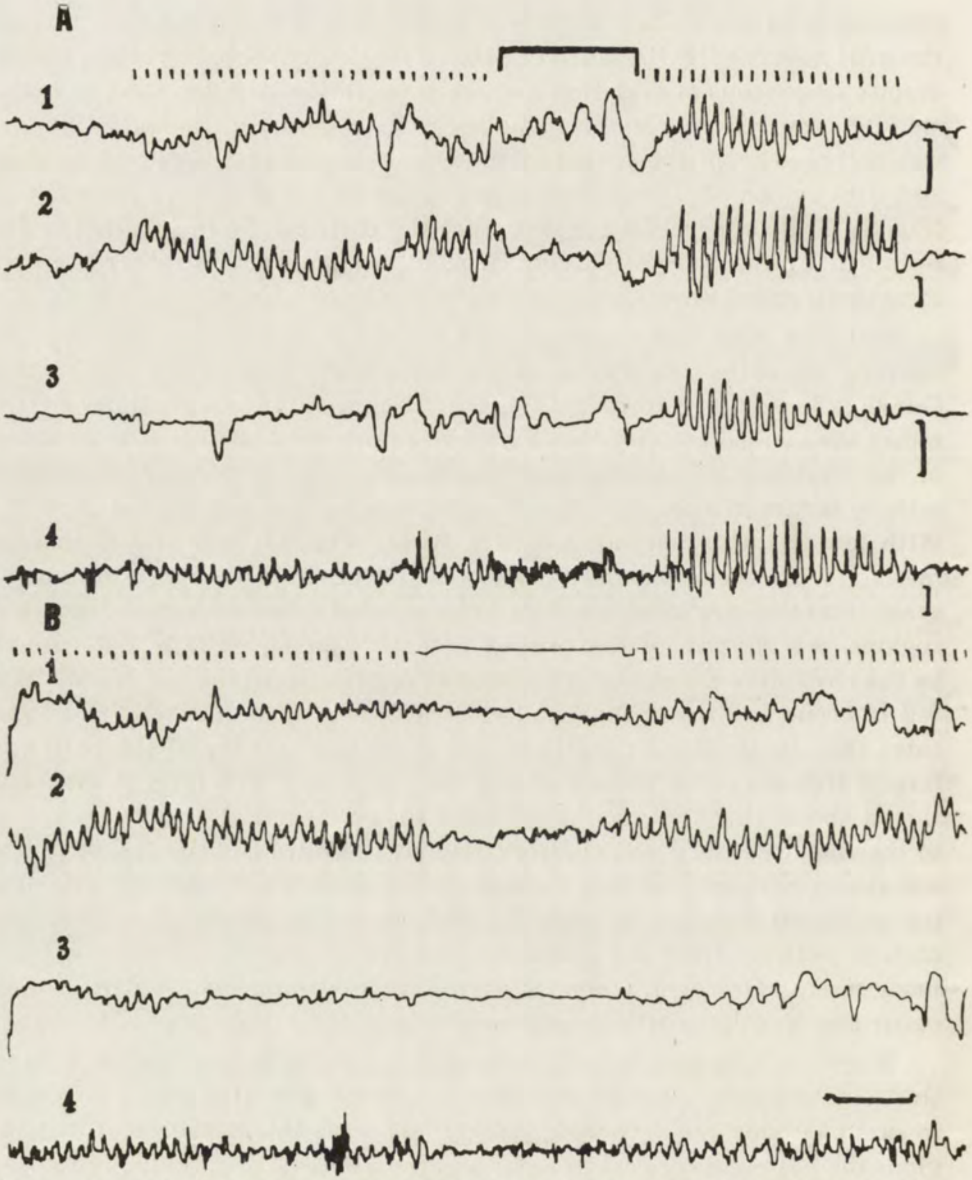

Fig. 6. Amplification of RR discharges following tetanization of the centromedian nucleus

Cat "Ban". Date: May 29, 1965. Recording electrodes on the somatosensory region: 1, left, bipolar; 2, left, monopolar; 3, right, monopolar; 4, right, bipolar. A, the cat is asleep; stimulation rate 7/sec. (0.2 msec., 45 v.). Upward movement in the signal line indicates an increase in the rate to 70/sec.; the cat awoke and began to move. The depression in the signal line indicates a decrease of the rate, back to 7/sec. B, stimulation at a frequency of 7/sec. was followed by a break of 2 sec.; thereafter, the stimulation was given again. The cat slept, no behavioral responses occurred. Time: 1 sec. Calibration: 50 microvolts.

a reduced amplitude) than in sleep, exhibiting a slow electrical activity in the cortex. Sometimes, it ceased to occur at all even when the strength of the stimulation was sufficient to produce a clear-cut RR activity in the sleeping state, or it was maintained in a reduced form in some cortical regions (usually in those in which the amplitude was large in sleep) and disappeared entirely in others, i.e. the RRs underwent a concentration being limited to some cortical regions. We have also observed a definite decrease of the RRs in deep sleep which was associated with a fast electrical activity in the cortex.

As pointed out previously (cf. the introductory part of this paper), a decrease of the RRs in normal animals can be produced by electrical stimulation of the brainstem reticular-formation and when acoustic stimuli are used. As illustrated in Fig. 5A, acoustic stimulation in a sleeping cat exerts a clear-cut reducing effect on the RRs in the somatosensory regions and suppresses the RRs in the acoustic and suprasylvian regions. A similar observation was made when the cat was awaken by calling it (Fig. 5B). Fig. 5D shows that the RRs were also markedly reduced when the cat opened its eyes voluntarily. As seen in Fig. 5C, the RRs can be prevented when the animal is awaken by calling it just after the onset of the NTS stimulation, that is prior to the occurrence of the RRs; when the animal closes its eyes, the RRs may be elicited. A sleep-producing low--frequency stimulation of the NTS was associated with behavioral drowsiness (see below). Conversely, stimulation at a frequency of 50—100/sec. produced behavioral arousal; the animal raised its head, looked about and attempted to escape. EEG arousal was obtained following high-frequency stimulation of the NTS (Fig. 5F).

By varying the rate of the shocks applied to the NTS variations in the behavior pattern were produced. Fig. 6A shows an experiment with increasing the frequency from 7/sec. to 70/sec. and then decreasing it to 7/sec., the RR potentials bocome markedly amplified after tetanization; this amplification is clearly seen because — as pointed out previously — RRs are reduced during EEG activation; this indicates that an amplification in the RR potentials within 2—3 sec. following tetanization is not induced by the arousal. Such observations were not made when 7/sec. stimulation was interrupted for 2—3 sec. Usually, the RR potentials to the second stimulation displayed the same amplitude as prior to the break in stimulation (Fig. 6B).

When the centromedian nucleus was stimulated we recorded the RRs also from the midbrain reticular formation Under these conditions, the RRs were elicited in the form of „bursts" (Fig. 7A), or, after the initial increase they occurred uniformly (Fig. 7C). It is to be noted that the RRs evoked in the reticular formation were often different from those which were elicited in the cortex, the initial increase of the RRs in the reticular formation being faster. It was shown that an increase in the stimulation frequency to 12/sec. was associated with a slight diminution of the RRs in the reticular formation and a clear-cut diminution or abolition of the RRs in some cortical regions. This indicates that the RRs are elicited in the reticular formation and in the cortex independently. It was found that high-frequency stimulation produced slow waves, 2—3 per second (Fig. 7B).

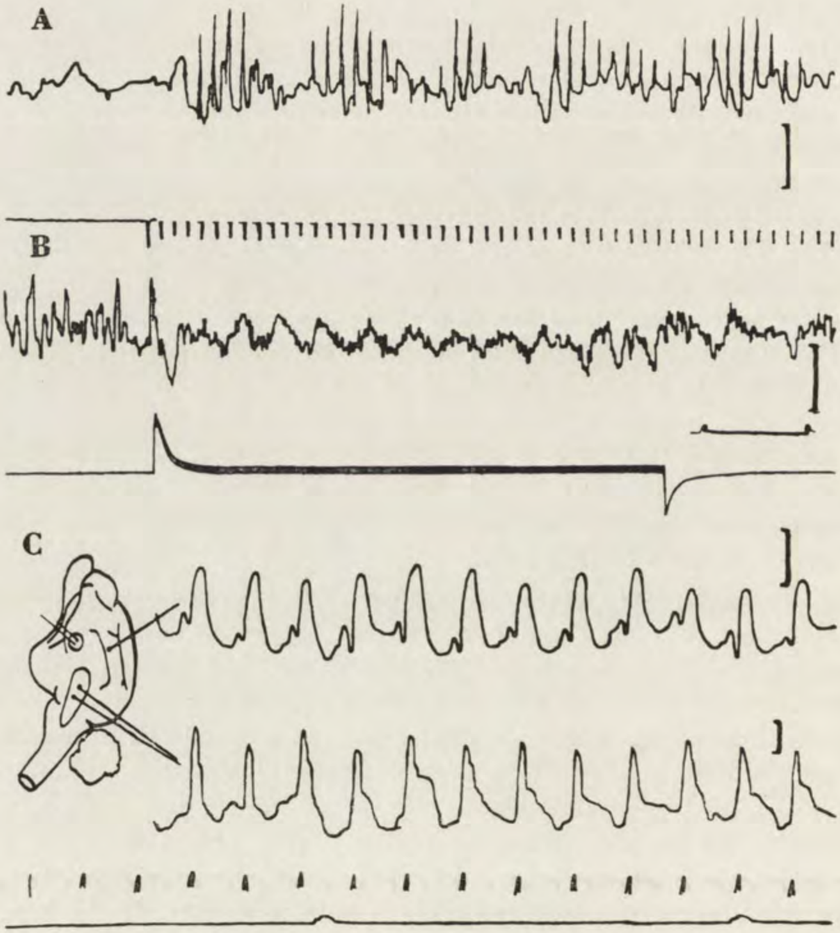

Fig. 7. The RR of the midbrain reticular formation.

Cat „Gan". Date: May 13, 1965. A, discharges in the reticular formation in response to the stimulation of the centromedian nucleus (7/sec., 0.5 msec., 20 v.). The cat is asleep. The stimulation was not associated with any behavioral response. B, stimulation at a rate 100/sec.; the cat awoke. C, discharges recorded from the cerebral cortex and the reticular formation to the stimulation of the centromedian nucleus of th sleeping cat (7/sec., 0.5 msec., 20 v.). The placement of the stimulating and recording electrodes is indicated. Time: 1 sec. Calibration: 100 microvolts.

If stimulation was of moderate strength but sufficient to produce the RRs in the cortex no motor reactions were elicited. Such stimulation often produced drowsiness if the cat had been in the waking state, or deep sleep if the animal had been in the stage of an ,,early" or light sleep. This sequence of behavioral events was associated with characteristic shifts in the frequency pattern of the EEG. Fig. 5E shows that 3—4 sec. stimulation was sufficient to cause a shift to slower frequency. As seen in Fig. 8A, there is a swing from a waking to a drowsy and sleeping state within a few seconds: the animal closed the eyes, began to purr and, finally fell asleep. The termination of motor activity is another characteristic reaction associated with the NTS stimulation at a frequency of 6 to 12 per second: the animal stopped performing the ,,voluntary" motor act, stopped drinking milk (Fig. 8B), eating meat, approaching the food cup when this was uncovered or when an acoustic conditioned stimulus was given; it refused to

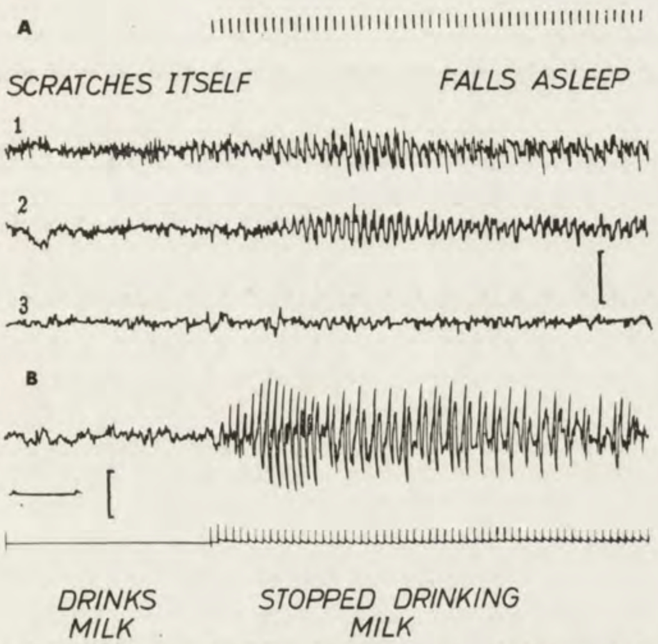

Fig. 8. A correlation between the RRs, the occurrence of sleep and the suppression of motor activity.

A, cat "Ban". Date: March 29, 1965. Recording electrodes: 1, left somatosensory region; 2, right somatosensory region; 3, left acoustic area. Stimulation of the right centromedian nucleus. Before stimulation, the cat was active and scratched its body. With the onset of the stimulation the cat stopped scratching and began to fall asleep. B, cat "AN". Date: December 14, 1963. The potentials were recorded from the parietal cortex. With the stimulation of the centromedian nucleus (8/sec., 0.5 msec., 10 v.) the cat stopped drinking milk. Time: 1 sec. Calibration: 50 microvolts in A, and 100 microvolts in B.

respond with a motor reaction when external stimuli which used to elicit an orienting reflex were presented. Our experiments have shown that the motor reaction, which had stopped upon a low-frequency stimulation of the NTS, recovered when the stimulation was terminated. This was noticed even under conditions of the stimulation persisting for a period of many seconds: the animal went on with the motor reaction as if nothing had happened. Of special interest is the observation that after a series of day per day NTS stimulations the animal became somnolent whenever it was placed in the testing cage. Sleep induced to the NTS stimulation was very deep and the animal could be hardly awaken. These effects have been more readily obtained from the stimulation of the reticular nucleus than from the stimulation of the centromedian nucleus.

DISCUSSION

Electrical brain responses induced in the above experiments occurred as a consequence of unnatural stimulation to the central nervous system. Hence, they are only of relative significance for understanding the NTS function. Strong 6 to 10 stimuli delivered to the centromedian nucleus produce stereotyped potentials at all the recording sites of both the cerebral cortex and the midbrain reticular formation, the „spontaneous" electrical activity being suppressed. Thus, under these conditions the electrical activity of the cortex may be considered to be largely a result of the stimulation of the nonspecific nucleus. On the other hand, moderate stimulation evokes either recruiting responses showing considerable variation in the shape, amplitude, latency and pattern: a „burst" activity, or a continuous train of discharges with no signs of periodicity. The RRs depend on both the previous NTS stimulation and the conditioned-reflex activity occurring to the general aspects of the experimental situation. The instability of the RRs under chronic conditions is the basic feature of the normal animal's activity which has not been observed in an anesthetized animal.

Our findings show that the centromedian nucleus is anatomically associated with the midbrain reticular substance and that these associations contain fewer synaptic relays than those between the centromedian nucleus and the cerebral cortex. This is in a good agreement with the data obtained in acute experiments (Schlag 1958, Schlag and Faidherbe 1961) and supports the morphological evidence pointing to a descending pathway from the NTS to the midbrain and bulbar reticular formation regions, originating in the parafascicular complex (Leontovich 1959). Schlag et al. (1961a,b) have found that after termocoagulation of the posterior commissure the NTS stimulation fails to produce the RRs in the lower portions of the brain stem. Following such lesion, high-frequency stimulation of the NTS does not produce the „alerted" pattern of the cortical electrical activity as that illustrated in Fig. 5F. On the contrary, under such conditions sfimulation at a rate of 100 per second results in slow wave activity in the cortex (Schlag et al. 1961a,b, Schlag and Chaillet 1963). These observations lead to the conclusion that the „alerted" pattern of the cortical electrical activity evoked by high-frequency NTS stimulation is not a consequence of the excitation of the NTS, projecting on the cerebral cortex, but occurs as a result of the excitation via thalamoreticular pathway of the activating system of the brainstem.

Weak stimulation of the centromedian nucleus elicits the RRs only in the homolateral somatosensory region. When the stimulation intensity is slightly increased the RRs spread over the parietal region. In other words, an intensification of stimulation is associated with an irradiation of RRs in the cortex Presumably, an intensification of stimulation leads to widespread excitation of the NTS, different portions of which are, apparently, interconnected with different regions of the cerebral cortex. It must be emphasized, however, that despite stable stimulation conditions, the distribution of RRs is found to vary from one experiment to another. On the other hand, external stimuli may limit the distribution, sometimes. This shows that „irradiation" and „concentration" of the RRs over the cortical surface are a function of the continuously varying physiological states of the central nervous system. We have failed to show a clear-cut „irradiation" of the RR activity when longlasting and repetitive stimulation was applied to the centromedian nucleus. Perhaps, this may be achieved with the stimulation of other NTS nuclei. The relation of the phenomena described to the inhibition process travelling over the cerebral cortex will be considered in a later paper.

The variation of the RRs appears to be associated with the wakefulness level. This concerns both the character of RRs (Yamaguchi et al. 1964) and, as pointed out previously, their distribution over the cortex. Varying degrees of wakefulness can often be associated with the sensory stimulations. However, if the NTS is stimulated not only does the efficacy of the stimulation depend on the state of wakefulness but, presumably, the state of wakefulness varies with NTS stimulation.

Roitbak (1958, 1962) presented evidence showing that NTS stimulation at a rate of 8—12/sec. leads to drowsiness and to the suppression of motor activity and sleep. Recent findings have confirmed this observation. It has been demonstrated that stimulation of the NTS in unanesthetized cats inhibits locomotor activity occurring spontaneously or in response to the stimulation of the subthalamus. Furthermore, it has been found that an inhibition of induced motor activity follows NTS stimulation in decorticated cats. A possible explanation then is that inhibition is not necessarily localized in the cerebral cortex. It is nonetheless quite likely that in intact animals inhibition of motor activity following NTS stimulation is initiated in the cortex (Grossman 1958). Hösli and Monnier (1962) have shown that stimulation of the NTS (3—12/sec., 0.7 V, 12 msec.) in rabbits produces behavioral sleep in association with delta rhythm. The same is true of the NTS stimulation in cats (Yamaguchi et al. 1963, 1964). On the other hand, a bilateral damage to the NTS in the rabbit results in hyperactivity (Hösli and Monnier 1962).

NTS stimulation associated with the RR activity in the cortex may serve as a conditioned stimulus for an avoidance response (Angyan et al. 1963) or a classical motor-defensive conditioned reflex (Sakhiulina and Merzhanova 1963, 1964). It is of interest that under these circumstances an inhibition is present as well: the conditioned reflex usually fails to occur during the conditioned stimulation but it does occur when the stimulation is over. Furthermore, such stimulation leads to drowsiness asociated with an inconsistent conditioned-reflex activity (Angyan et al. 1964, Sakhiulina and Merzhanova 1964). So far, it has not been possible to show an inhibition of a food-reinforced conditioned response in cats (Sakhiulina and Merzhanova 1965), or a classical motor-defensive conditioned reflex in monkeys (Pecci-Saavedra and Doty 1964). The evidence for behavioral alterations following NTS stimulation associated with RR activity in man is somewhat tenuous. Thus Housepian and Purpura (1963) report no effect of NTS stimulation on human behavior, while Jung (1957) finds evidence of dreaming and true sleep. Grastyán et al. (1965) have shown that, depending on the experimental conditions, the electrical stimulation of the centromedian nucleus may lead to opposite behavioral alterations.

Altogether, the most recent experimental evidence, including that of the present paper, supports the earlier data indicating that (1) the NTS and brainsten reticular formation serve different functions, and (2) the NTS is an organ associated with inhibition (Grastyán et al. 1954, Roitbak 1958, Monnier et al. 1960, Magoun 1963). Results obtained in microelectrode experiments in which discharges from single cortical neurons are recorded during the NTS stimulation (under acute conditions) favor the view of the important role of the NTS in inhibition. It was found that when stimulation of the NTS results in sleep, 77 per cent of recording neurons did not fire; on the contrary, 60 per cent of neurons were found to be firing during high-frequency NTS stimulation associated with the state of wakefulness (Krupp and Monnier 1963).

Magoun (1963) has suggested that there is a reciprocal inhibitory interaction between the NTS and the activating brainstem reticular system. This has fitted with our finding, showing a striking increase of the RRs after a high-frequency stimulation of the NTS. As pointed out previously, a high-frequency stimulation of the NTS aroused the animal due to the excitation of the brainstem activation system. Obviously, an increase in the RRs is a manifestation of the postinhibitory facilitation. This after-effect is strong enough to compete with the state of wakefulness of the animal. However, it cannot be considered a consequence of post-tetanic potentiation because of the absence of depression phase after the tetanization, and because the after-effect was too short.

Beritoff (1937) advanced a hypothesis that alpha waves were a result of the neuropil activity and exhibited an anelectronic inhibitory influence on the cortical cells. Beritoff and Roitbak (1955) suggested that the activity of the apical dendrites of the pyramidal cells caused a presynaptic inhibition. Jasper (1960) considered the surface negative RR potentials to be manifestations of dendrite excitation. Intracellular recording of cortical neurons during the RRs has revealed a depolarization of some neurons and hyperpolarization of some others (Purpura and Shofer 1964). Quite possibly an inhibition following the NTS stimulation is associated with negative DC shifts rather than with the RR activity (Goldring et al. 1958). Storh et al. (1963) have shown that the slow surface negative potentials coincide with a decrease of discharges of the cortical cells. Roitbak (1963) considers the long--lasting negative potentials to reflect a depolarization of the apical dendrites due to the activation of the surrounding neuroglia. In Roitbak's view (1965), this glia-dentritic system of the cerebral cortex is excited by impulses carried via the nonspecific afferents.

SUMMARY

In cats with chronically implanted electrodes electrical potentials from both the cortex and the midbrain reticular formation were recorded upon the stimulation of the thalamic centromedian nucleus; in addition, changes in behavior pattern were noted.

If 6—10 shocks are delivered each second a recruiting response occurs in both the cortex and the midbrain reticular formation. In normal cats, the recruiting waves show a considerable variation of the amplitude, shape and distribution over the cortex. Both „irradiation" and „concentration" of the recruiting activity are found to occur. The recruiting activity diminishes in response to peripheral stimulation. Fifty to 100 shocks per second delivered to the centromedian nucleus produce arousal and may lead to the occurrence of slow (2—3/sec.) waves in the midbrain reticular formation. Following a high-frequency stimulation of the nonspecific thalamic nucleus shocks delivered at a rate of 6—10 per second produce a 2—3 sec. increase in the RRs. The recruiting pattern is associated with the somnolent state and suppression of the animal's motor activity. This is seen more clearly with the stimulation of the reticular nucleus than with the stimulation of the centromedian nucleus. The relation of the inhibitory action of the nonspecific thalamic system to the cortical surface negative potentials which are, presumably, of the glia-dendritic origin, is discussed.

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TRANSISTORIZED PROGRAMMING SYSTEM FOR A VISUAL DISCRIMINATION TASK[1]

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In this paper the programming system for the final stage of an experiment will be described. Elementary transistorized logical units[2] have been used to build a system which presents stimuli, records the responses and delivers the reinforcement. The system *in toto* has been described, of particular interest are some solutions in it, e.g. the economical way of random presentation of discriminanda, the response filtering block, and the response classifier. It is assumed that the readers are familiar with the basic principles of digital logic. Comparison of the detailed and block diagrams will be helpful in separating out parts of the system.

The aim in the task is to teach animals to expect a short-lasting presentation of discriminanda, to notice them, and to respond appropriately in order to obtain a food reinforcement. The trial begins, after an interval of unpredictable duration, with a sound stimulus (a tone) lasting randomly from two to five seconds. At the very and of the stimulus presentation a pair of different visual patterns is displayed for a very brief time and the animal is required to press the transparent plate in front of the correct pattern within twenty seconds in order to obtain food. Time relationships are presend in Fig. 1.

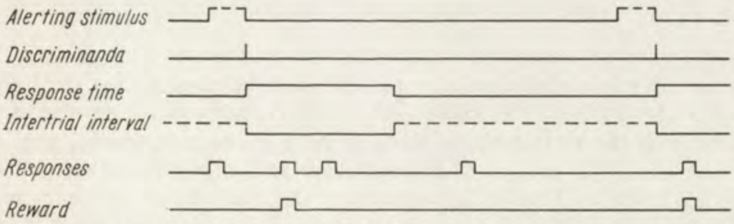

Fig. 1. Sequence of events in each trial. Broken line represents variable duration

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[1] This project has been aided by a grant from the Foundations' Fund for Research in psychiatry to the second author who is presently at the Nencki Institute in Warsaw.

[2] Digibits made by BRS Electronics, Beltsville, Md., USA.

The session starts when the experimenter lets the impulses from the clock go into the ratio programmer[3] the tape of which is perforated so that the contact closes at random intervals twice within each trial. Distances between the holes in each pair and between the pairs are calculated to give unpredictable durations of the tone and the intertrial intervals, respectively. The first signal sets the FF (3) into the position which switches on a 2000 cps multivibrator and opens the gate into the loudspeaker thus producing sound. Impulses from this multivibrator go also to the FF (6) which determines the position of the discriminanda. The second signal from the ratio programmer has a number of functions. First, it goes to the counter (2) which will terminate the session after the 32nd trial. It also terminates the sound as well as filling of the FF (6) which then remains randomly in one of the two possible states determining the *position* of the discriminanda. The same signal triggers two monovibrators, one (5) determining the *duration* of the discriminanda display and the other (10) the maximal time during which the correct response will be reinforced. It also resets the FF-s in the response-filtering block. There is a separate FF (8) which remembers the position of the discriminanda in the preceding trial and this information is used in the response-classifier block to determine correctness of the response.

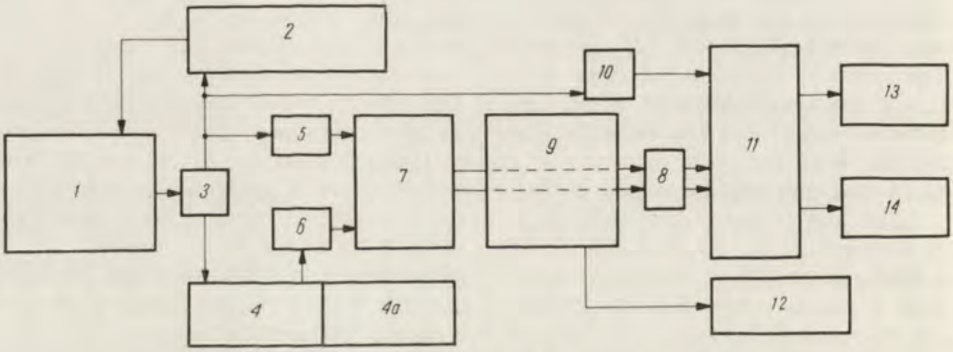

Fig. 2. Block diagram of the programming system

3: Flip-flop sending odd signals to the multivibrator 2000 cps, and even signals to the rest of the system. 5: Block determining the duration of the discriminanda display. 6: Block determining the position of the discriminanda. 8: Memory for the discriminanda position in the preceding trial, used in response classification. 10: Response time determining unit.

Any press of the two transparent plates is a response. At the beginning of the discriminanda display both FF-s in the *response-filtering block* (9) are in the initial state. By pressing any of the plates the animal changes the state of one of the two FF-s, it opens one AND-gate in the same block and closes the other. Thus the response-filtering block is irreversibly set until the next trial. Another press of the same plate does not change anything (it goes only into the „total" counter), and the signal produced by the press of the other plate does not go through the closed corresponding AND-gate. In this way during each trial, provided the animal responds in the due time, it is possible to make only one response which would be

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[3] Ralph Gerbradt's RP SHS.

classified either as correct or as incorrect. A response is correct if the animal presses the plate in front of the „correct" pattern which randomly changes place. The response-classifying block consists of four AND-gates and two OR-gates. In each trial only one AND-gate may be opened. OR-gates are connected with recording devices and the food dispensary. All responses including correct and incorrect ones are counted in the „total" counter. Simple subtraction gives the number of „extra" responses.

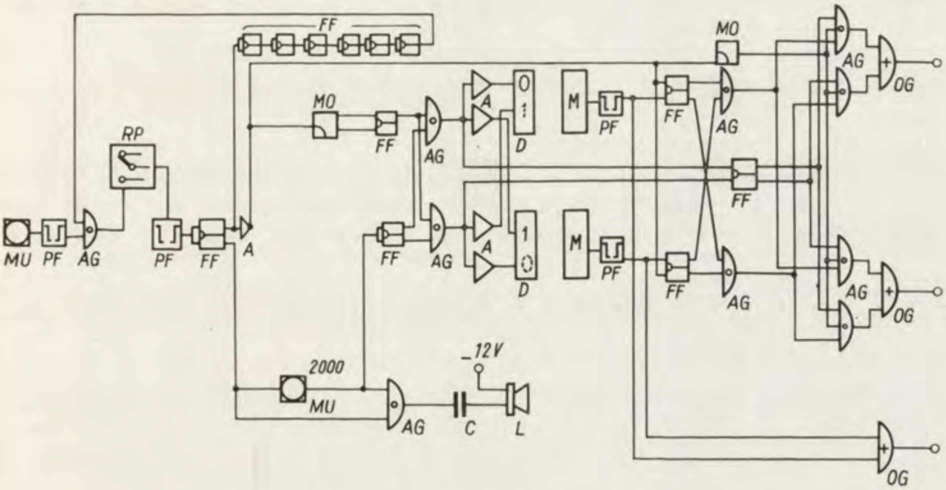

Fig. 3. Detailed diagram of the programming system.

Multivibrator (MU), produces series of pulses of adjustable frequency.

Pulse former (PF), transforms the deformed into well shaped pulses.

Ratio programmer (RP), a slowly turning wheel which drives a circular perforated tape through the holes of which pulse producing constacts are made; the holes are punched at the predetermined distances.

Flip-flop (FF), one of its halves is on one, and the other half on the other potential level; each incoming pulse reverses the situation; different ways of feeding in the pulses allow different ways of using flip-flops.

Monovibrator (MO), delivers pulses of approximately (precision is relative here) the same duration no matter how long was the incoming pulse.

AND-gate (AG), there is an output only if there are inputs on the all input „legs" simultaneously.

OR-gate (OG), there is an output if there is an input on any of the „legs".

Amplifier (A). Condensor (C). Loudspeaker (L). Manipulanda (M). Discriminanda (D).

We agree with Weiner (1963) that the elementary logical units are reliable and flexible, but they require some sophistication to a great extent independent of that obtained from working with relay circuitry.

SUMMARY

A programming system made out of transistorized elementary logical units has been described. It was designed to program a visual discrimination task. Some solutions in the circuitry may appear useful in similar setups, particularly the response-filtering block as well as the way in which random presentation of the discriminanda has been obtained.

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Book reviews

The foundations of genetics by F.A.E. CREW, F.R.S. The Commonwealth and International Library. Zoology Division. General Editors: J. M. Dodd and Sir Francis Knowles. Published by Pergamon Press, Oxford 1966, 202 pp., 7 plates, 23 figures. Price: 21 s.

The book by Dr. F.A.E. Crew, a former Professor of Animal Genetics in the University of Edinburgh, makes up a review of the development of genetics from pre-Mendelian times, through the achievements of John Gregory Mendel, T. H. Morgan and others, up to a brief outline of the present state of this science.

A historical presentation of the development of genetics with a particular stress laid on its elements which constitute a contribution to science was the author's aim. In addition, the author intended to attract the readers' attention to the profiles of investigators and founders of the most eminent genetic theories.

Professor F.A.E. Crew's book is remarkable as a rich source of information, both genetic and historical. Its structure is marked by a strict discipline and consistency in the presentation and expression of thoughts. The clarity and comprehensibility of the problems, shown in simple, logical correlations, are indubitable values of this book. The figures, enclosed with the text, excellently illustrate the problems discussed and provide a valuable aid for the reader.

The chapters of F.A.E. Crew's book are devoted to the following problems: (1) The description of the development and of the motives of activities, undertaken by people who, in pre-Mendelian times, tended to obtain — in domesticated animals and in cultivated plants — a number of features which might be utilized for practical purposes. This chapter also contains a discussion of the terminology, related with the heredity as understood in the historical aspect. (2) Gregory Mendel as a man and investigator. (3) Mendelism. In this chapter, the author introduces the readers to the work and achievements of the founder of the law of segregation and the theory of the corpuscular elements that determine the hereditary characters. Furthermore, he presents the profiles of Gregory Mendel's predecessors and contemporary investigators. (4) The history of the rediscovery of Mendel's laws. (5) Further studies on the heredity, the confirmation and misinterpretation of Mendel's laws. (6) The theory of the gene. The relation of Mendel's and his successors' findings to cytology. The triumph of Morgan's theory. (7) The nature of the gene and the mode of genic action. A brief outline of most recent achievements in the field of the molecular genetics. (8) The review of the ramifications of the classical genetics, related with the specialization or with particular manners of its application, such as, animal and plant genetics, hybridization, cytogenetics, polyploidy, eugenics, biochemical, medical, radiation and human genetics, as well as the problems that result from the analysis of the laws of heredity as an element of evolution.

The author refers to over 60 items of the source literature. In addition, he gives a list of 14 original papers and 88 monographs (pp. 189—193) which make up a literature supplementary to the information, contained in particular chapters. The book is also provided with indexes of the terms and authors cited.

In view of a rapid development, specialization, and accumulation of new facts in the field of genetics, giving the readers a monograph that might fully exhaust the topic (defined in the title of F.A.E. Crew's book) became impossible. For this reason, the author gave relatively more information which is historical in character and now almost unavailable in the form of sources and less information on the present stage of genetic studies and on the present-day investigators.

A manner of giving definitions and terms makes up a particular advantage of F.A.E. Crew's book, the more so for the readers who are not conversant with the genetic problems and terminology. In addition to his clear and unequivocal formulations, the author gives several explanations, as well as the roots of the terms used.

The review of the developing specializations and ramifications of genetics may interest the biologists by a wide extent of the problems and trends to which genetics gained access and was applied.

It would be hardly possible not to mention humane aspects, resulting from the reading of this book. F.A.E. Crew puts emphasis on them in the history of genetic discoveries.

The elaboration of such a difficult subject, requiring the knowledge of both genetics and hitory of the facts described makes up a great merit of the author of the book reviewed.

Jerzy Sikora, Warsaw, Poland

Leitfaden der Anatomie der Wirbeltiere (*Outline of the Anatomy of Vertebrates* by L. KÄMPFE, R. KITTEL, and J. KLAPPERSTÜCK. Published by VEB G. Fisher Verlag, Jena 1966. 2nd, revised and extended edition. 322 pp., 187 figures, 4 tex tables. Price: 22. 80 MDN.

In observing the development of some branch of science, we may easily notice that it always begins with revolutionary discoveries and ideas, hereafter, passes into a longish period of a strained work, done by many investigators who collect facts and develop a theory and, finally, it is systematized in big, multi-volume textbooks. During the latter, „mature" period, there also appear many less extensive, semi-popular textbooks whose aim is to put this knowledge within easy reach of those interested in a given subject. The book reviewed, intended (according to publishers' prospectus) for university students, assistants, associates and professors of zoology, teachers of biology, as well as specialists in evolution and classification, is precisely such a textbook of comparative anatomy.

A basic scope of the knowledge of anatomy is shown by the authors in eleven chapters, presenting particular sections of anatomy. Moreover, according to the tradition, they do not confine themselves to the vertebrates only but also include the descriptions of the organs of the lancelet and even of the tunicates (Tunicata). The book opens — if we skip a brief taxonomic review — with a chapter, devoted to embryology which contains elementary embryological concepts, as well as the fundamentals of the development of the lancelet and other chordates. The text is illustrated with diagrammatic figures in which, for instance, the process of the formation of embryonic membranes or the differences in gastrulation of different mammals are visualized. Unfortunately, these figures are black-and-white, while a color print would be much more commendable.

The skeletal and muscle system is discussed in the next, most extensive chapter, making up nearly 1/4 of the entire text. Particular parts of the skeletal and muscle system are presented in it in a concise and, at the same time, clear manner. Not entering into a discussion, the authors try rather to collect and confront facts and it is with much caution that they present the theories, as, for instance, that on the formation of the extremities. The text is illustrated with many figures. However, the lack may be noticed of the diagrams of the neurocranium, of the reptile skull and of the development of auditory ossicles in mammals. Relatively much space is devoted in this chapter to the muscles which in other similar publications are frequently treated too superficially.

The other four chapters contain the descriptions of internal systems, that is, of the digestive tract, respiratory, circulatory, excretion and reproduction and internal secretion (endocrine glands) systems. Like in previous chapters, there is a rich collection of facts and confrontations, illustrated with simple diagrams. It is also in these chapters that colored plates, in particular to present the circulation, would be advisable. As concerns the extent, most space is devoted to the circulatory system and least to the endocrine glands.

The chapters on the nervous system and sense organs are the most interesting ones from the neurophysiologist's standpoint. Totally, they make up about 20 per cent of the entire text. The basic information is given on the nerve physiology and on particular sections of the central nervous system, beginning with the spinal cord. In this respect, the authors have faced a difficult task of presenting a very extensive material on few pages which resulted in a rather superficial description without a thorough analysis of the brain function. Moreover, in this chapter, there is not a single figure which might illustrate the nerve pathways and centers and thus supplement the text which, of necessity, is very brief.

Surprisingly enough, the description of the nervous system is supplemented by the chapter in which the sense organs are discussed and which exceeds by four pages the chapter on nervous system. Obviously, this decreases the clarity of the material presentation. The chapter, devoted to the skin and its derivatives in which this section of anatomy is fairly extensively discussed, closes the contents of the book.

To sum up, the book by Kämpfe, Kittel and Klapperstück is of a principal interest to scientific workers concerned with biological problems. Its clear and comprehensive German makes up a very valuable property of this book, especially so for the foreign readers.

Jerzy Kreiner, Cracow, Poland

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