BEHAVIOURAL AND ELECTROPHYSIOLOGICAL CORRELATES OF DISCRIMINATION LEARNING: NEW EVIDENCE FOR SELECTIVE NEURAL PLASTICITY IN SENSORY SYSTEMS.

Dr. Mohamed BELLOUM
University Biskra

Abstract:

The general aim of this experimental psychological research, on the behavioural and electrophysiological correlates of discrimination learning, is to prove the existence of durable associative mechanisms (i.e stable neuronal conditioned responses) in the sensory-specific areas of the auditory system[*1] . It aims also to show that these associative mechanisms could reflect stimulus habituation & expectancy phenomena as well as selective filtering & gating of information (at the peripheral level), that, may depend on conditioned emotional response effects (CER effects) & /or frustrative non-reward effects (often predominant during avoidance or aversive instrumental learning with delayed reinforcement) on the one hand, and on the centrifugal influence of the hippocampus as comparator of information during two process discrimination learning[*2] , on the other hand.

ملخص:

الهدف العام من هذا البحث النفسي-الفيزيولوجي التجريبي للعلاقات السلوكية والإلكتروفيزيولوجية المتبادلة خلال التعلم التميزي هو برهنة وجود آليات إرتباطية دائمة (أي إستجابات إشراطية عصبية ثابتة) على مستوى النواحي الحسية المختصة من الجهاز السمعي3*. ويهدف البحث أيضا الكشف على أن هذه الآليات الإرتباطية بإمكانها أن تكون مصدر الظواهر التعود والترقب للمثير والتصفية الإنتقائية (أو الغربلة) للمعلومات (على المستوى المحيطي). مع العلم أن هذه الظواهر يحتمل أن تكون بدورها متعلقة بأثر الإستجابات الإنفعالية الشرطية (كثيرا ما تكون مسيطرة خلال التعلم التميزي المتعلق بالتجنب أو الخوف)* من جهة، و يتأثير الغربلة الطاردة من المركز للهيبوكمبس (Hippocampus) كجهاز مقارنة للمعلومات خلال التعلم التميزي ذو العمليتين (Two-process discrimination learning) من جهة أخرى .

***: و/أو أثر الامكافأة الإحباطية (Frustrative non-reward effect).**

***1: Considered up to now as sites principally involved in the coding & selection of information, or at most as short-term memory relays, but not as sites susceptible of engram formation.**

***2: cf. J.A.Gray (1975): p: 25, 28 & 287.**

3*: التي إعتبرت لحد الآن غير قابلة لتسجيل الذاكرة بصفة مستقرة ودائمة

INTRODUCTION:

The classical view that primary sensory areas of the brain are merely involved in the coding and representation of the physical characteristics of a stimulus has been questioned by findings from Gabriel et al (1975; 1976), Disterhoft and Stuart (1977), Olds et al (1978) and other investigators as well as by recent studies and experimental results from Edeline J.M (1990, 2002), Shulz, D.E (2002,2004), Tillmann, B(2003) & Kilgard, M.P & Merzenich(1998),.

That short latency learned responses can develop in sensory specific structures (e.g. LGN[1], MGN[2], inferior colliculus, etc…) is a well established fact. What has not yet been clearly established is the nature and origin of these changes; whether they are short-term or long-term changes and whether they are local or secondary to more peripheral alterations. This also raised the question of whether short-latency discriminative unit responses were indicative of the locus of the engram in the brain or just due to a biasing influence from a distant neural locus (Gabriel, 1976). In the case of the latter hypothesis, the source of the possible tonic bias stayed unspecified despite speculation about centrifugal control by the cortex, the reticular formation or even lower levels of primary sensory pathways. This was mainly because no known study had unequivocally demonstrated that the “biased” associative neuronal activity was dependent upon the influence of some conduction pathway other than the afferent pathway to the responding neurone.

Different and often conflicting explanations were suggested for the possible mechanisms underlying such associative changes recorded for example from the MGN, the inferior colliculus or even the cochlear nucleus. There was a great discrepancy in the results about latencies of these changes, due possibly to the chosen experimental paradigm (classical conditioning or operant

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[1] - LGN: Lateral Geniculate Nucleus.

[2] - MGN: Medial Geniculate Nucleus.

conditioning; aversive or appetitive training; steady state or transition state experiments), to the way the data was analysed (in terms of amplitude discrimination and time-bin –analysis of the single unit neuronal responses or the multiple unit activity responses or in terms of evoked EEG responses, etc…) and/or the lack of cytological or morphological identification of distinct neurone populations within the same structure.

The main aims of this research are:

a) Study the electrophysiological changes during a delayed reinforcement schedule in order to determine the level of unit activity during that delay with special reference to neural correlates of the anticipation of the reward and to assess the effects of background contextual cues on auditory unit activity.

b) Show that primary sensory pathways in the auditory system (e.g. Inferior Colliculus and Medial Geniculate Nucleus) can exhibit learned (associative) multiple unit responses and that the latencies of these responses are usually very short.

c) Find out whether these associative changes represent local alterations, are secondary to more peripheral alternations, or reflect tonic gating (efferent control) by more central areas.

The results reported here indicated that response latencies of multiple units sampled from the Brachium of the Inferior Colliculus (BCI) and the dorsal midbrain reticular formation were less than 16 msec in most cases, whereas response latencies of ventral reticular formation neurones were between 16 msec and 32 msec, and that short latency (≤ 16 msec) conditioned discriminative responses displayed by primary auditory pathways (BIC & MGN) are likely to be long-term selective associative

changes unaffected by descending non specific associative cortical influences but likely affected by nucleus basalis neuromodulation (Kilgard, M.P & Merzenich, M.M; 1998) and/or septo-hippocampal centrifugal stop mechanisms as well as hippocampal Theta (Θ) sensorial damping and gating associated with Conditioned Emotional Response Effects, or Frustrative Non-reward effects in Approach-Avoidance Discriminative Operant task.

PART I

Delayed Reinforcement Effects On Behavioural And Neuronal Activities: Expectancy, Attention And Purposeful Behaviour Versus Tonic Arousal And Stereotyped Behaviour:

1. Research aims and preliminary hypotheses:

A first set of experiments, using a delayed reinforcement schedule, were aimed at determining whether the rerouting of learned information in the nervous system, during steady state learning, induces recordable electrical changes reflecting expectancy of the reinforcement. This pilot experiment was performed to determine the pattern of firing of auditory and midbrain neurones during lever pressing for food with delayed reinforcement. Attempts were made to test the hypothesis that midbrain reticular neurones increase their rate of firing with the animal's readiness for the reward (Olds et al, 1969; Olds, 1969).At the same time multiple unit activity (MUA) was recorded during different manipulation of the experimental environment to assess the effect of background contextual cues on auditory and reticular unit activity during appetitive training. MUA was also observed during free reinforcements, tone and click stimulations, drinking, eating and other behaviours. Multiple units were sampled from 33 probes. Of these 33 probes, 6 were in the superior colliculus, 11 were in the dorsal part of the midbrain reticular formation, 4 were in the ventral part of the midbrain reticular formation, 6 were in the brachium of the inferior colliculus (BIC) and 4 were in the medial geniculate nucleus (medial subdivision).

2. Research methods and procedure:

The animals used in this pilot experiment were five (05) male rats of the Sprague-Dawley strain. The experimental technique, electrophysiological apparatus, training equipment and conditioning procedure used in this experiment include a cylindrical perspex cage as Skinner box, moveable micro-electrode assembly for electrophysiological recording of neuronal activity during free movements of the animal, electronic equipment (F.E.T head plug, wide-bandpass amplifier, commutator, filters and window discriminator, computer, 7-channel thermionic* tape- recorder, two-channel storage Tektronix oscilloscope, etc...etc) for data acquisition and analysis, and stereotaxic equipment and surgical equipment (probe implantation, blocking and sectioning equipment) for micro-electrode implantations and histological procedures [for more details see M.Belloum (1979): Behavioural and Electrophysiological Correlates of Discrimination Learning. Ph. D-Thesis University of Manchester (Chap II) : pp:36 to 62]

3. Results and discussion:

a- observed behavioural constraints and behavioural correlates of delayed reinforcement training schedule (observed behavioural results) :

During the first set of experiments (consisting of the pilot experiment) using a continuously reinforced delayed reinforcement schedule,[1] a number of behavioural correlates and phenomena were observed; namely that:

* Most animals developed a sort of polydipsia (excessive drinking between trials) when trained on the delayed reinforcement schedule. It appeared that they became increasingly “active” and “superstitious” (with marked stereotyped behaviours) during the first “noticeable” delay increase (likely from 0.25 sec to 0.5 sec).

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[1] - And a cylindrical perspex cage (as Skinner box).

* The animals seemed to learn to “wait” on the lever rather than “time” the delays. They often stayed on the lever beyond the delay used in the session.

* Typically all animals trained on the delayed reinforcement schedule made many succesive nonreinforced lever presses after the first failure to get a reinforcement (that is especialy if they previously received succesive reinforcements for succesive lever presses).

* During long delays (1.5 seconds and 2 seconds) most animals developed strange “superstitious” behaviours which came to “fill” the whole interval between the lever response and the reinforcement (e.g rearing, leaning on the lever, **licking the lever,** etc....)

b- Preliminary observed electrophysiological correlates of delayed reinforcement effects:

The results did not show any neuronal changes correlated with the anticipation of the reinforcement or with expectancy, but seemed to indicate that the specific auditory relays (e.g. MGN and BIC) may be subjected to some centrifugal inhibitory influence as a result of continual exposure to monotonous contextual stimuli, and could therefore be at the origin of coding and selective gating of information of a motivational character.

c- Detailed electrophysiological results and general discussion :

The finding that dorsal midbrain reticular neurones were closely related to head and neck movements is not surprising, since it is well known that the reticular formation is involved in occulomotor control (Azzena, 1966, Bender and Shauzer,1964).This however does emphasize the need for careful observation in order to rule out unit responses due to stereotyped behaviours rather than to learning or “attention” variables. It is noteworthy that neurones from the BIC did not seem to show any firing correlated with head or body movements.

The pattern of firing of MUA P3/12 in BIC and specially that of MUA P4/7 in MGN seen to suggest that both multiple units have acquired or had been subjected to, some tonic inhibitory function as a result of continual exposure to the BUN[1] . Responses to the turning off of the BUN may reflect dishabituation of the previously habituated "phasic" component of the arousal response, habituation of the "tonic" component having occured earlier (Sharpless and Jasper, 1956) due precisely to the lengthy exposure to the BUN(see Fig 4, 5a & 5b in Appendix) .

Although it is customarily believed that "phasic" habituation is mediated by the thalamic extention of the reticular formation (Sharpless and Jasper, 1956), it was recently suggest that the sensory relay nuclei themselves might be primarily responsible for this "phasic" habituation (Buchwald and Humphrey, 1973). Furthermore Wester (1971) reported rapid habituation of behavioural and electroencephalographic responses induced by discrete stimulation of the specific sensory nuclei in intact cats.

Holstein et.al (1969) observed spontaneous recovery of the habituated acoustic response following cessation of repeated auditory stimulation in the inferior colliculus and MGN. Similar results were reported by Altman (1960) and Kitzes and Buchwald (1969). Moreover spontaneous recovery in the specific sensory system is relatively rapid as is dishabituation. Thus, if on the one hand response decrements within the auditory pathway appear subsequently to habituation of the arousal response and on the other hand "phasic" habituation seems to be primarily mediated by sensory relay nuclei, what function is subserved by these sensory nuclei?

It can be said that when the arousal reaction induced by a novel stimulus habituates as the stimulus continues to be presented, the stimulus loses physiological

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[1] - Background Unit Noise.

significance to the organism and the responses it induces are simply “noise”. This noise can however be reduced as a consequence of response decrements of the auditory relay nuclei and higher levels would be freed for more complex processing of information.

As Buchwald and Humphrey (1973) put it “such a phasic decremental function would seem extremely well suited to the response characteristics of the sensory system itself “(rapid spontaneous recovery and rapid dishabituation) and... “ the sensory relays show no long-lasting “memory” for a repeated, nonsignificant stimulus but can damp the “noise” it intrejects into the nervous system until new significance is attached to it, as for example, by a dishabituating stimulus.” (Buchwald and Humphrey, 1973, p. 57).

The functional explanations given above for the observed patterns of firing of MUA P3/12 and MUA P4/7 are of course speculative.

As to the patterns of firing of ventral midbrain reticular formation neurones (MUA P3/14, MUA P3/15 and MUA P3/16) during lever pressing for food with a 2-second delayed reinforcement they may reflect either tonic neuromuscular responses, change in the arousal level or motivation dependent responses. Because of poor behavioural observations, it was difficult to unequivocally determine the cause of multiple unit responses.

4- CONCLUSION:

As multiple unit response increases correlated with head and body movements were mainly observed in the MGN, and dorsal part of the midbrain reticular formation, it is thus tempting to suggest that the initial increases in firing of ventral reticular units during most of the first second of the delay may reflect the incentive gradient along that delay. Indeed because of the past experience of the animals with shorter delays and because long delays of reinforcement reduce incentive (Spence,1956; Mowrer,1960), it is more likely that incentive would be higher at the beginning of the delay and lower in the middle and towards the end of the delay.

PART II

2. Short-Latency Conditioned Neuronal Responses And Behavioural Responses During Discrimination Learning[1]:

Phasic Versus Tonic Responses (Engram Or Bias ?):

1- Research aims and main hypotheses :

A second set of experiments were performed to investigated multiple unit response changes in the central auditory system of the rat during a tone signalled differential operant conditioning task. The main aim of these experiments was to search for short latency (<=16msec) conditioned neuronal responses as an evidence of associative mechanisms at the periphery of the auditory system or selective gating of sensory specific relays by non specific influences. In order to investigate possible anticipatory changes reflecting the S1-RF and S2-$\overline{RF}$ [2] contingencies and to separate neuronal changes due to arousal from those due to associative changes (i.e learned responses), multiple unit responses were recorded during two (02) different schedules of discrimination learning:

One in which tones were presented in a random manner on a 50% probability ratio schedule (PR. 50%).

The other in which series of successive reinforced trials (of the type S1 – RF) alternated with series of nonreinforced trials (of the type S2-RF) in a variable interval fashion (VI. 90 sec) .

.2- Research Methods And Procedure:

Twenty three (23) male Sprague-Dawley rats were trained to operantly discriminate between two tones S1 and S2 (of respectively

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[1] - With Tone Signalled Delayed Reinforcement.

[2] - I.E.S1 signalling reinforcement (RF) and S2 signalling no reinforcement (RF)

1kHz & 4kHz), one signalling the delivery of a food pellet and the other signalling nothing. Once all the animals have been overtrained on the tone discrimination schedule and operated for microelectrode implantation, behavioural and electrophysiological data were recorded during every 20 to 30 trial block. Daily sessions included between 100 and 200 trials. Reversal training was introduced to rule out neuronal changes due to the sensory characteristics of the tones.

In this second set of experiments, a two differently painted compartments –Skinner- like box (see Fig 1, Appendix), was used instead of the cylindrical perspex cage used in the first set of experiments. The first reason for this was to separate aversive effects due to the experimenter handling of the animal during the microelectrode manipulation & sampling of unit activity from appetitive training and testing sessions, the second raison was to be able to separately record at will neuronal unit activity during sleep, grooming, eating, drinking and exploratory behaviours on the one hand and conditioning trials on the other hand. The third reason was to allow for minimum generalization effects from one compartment to the other, and increase the saliency of the contextual cues during appetitive training sessions as a result of the contrast in configuration of the two compartments.

To sample and record unit activity from various brain structures of the animal, a moveable microelectrode device (see Fig 2, Appendix), slightly modified from that described by Vertes (1975), was used. The electrophysiological data consisted mainly of multiple unit activity (MUA), selected through a high pass filter (300 Hz, 500Hz or 1000Hz with a gain of 10) and a window discriminator within the recording system (see Fig 3, Appendix) [for more details see M.Belloum (1979): Behavioural and Electrophysiological Correlates of Discrimination Learning. Ph. D.Thesis University of Manchester. (Chap II pp: 36 to 62 and chap V and VI pp: 93 to 95 and pp: 110 and 111).

3. Results And Discussion:

a) Observed behavioural constraints and behavioural correlates during tone signalled discrimination operant learning:

During the tone signalled discrimination operant learning schedules (PR 50% & V.I 90 sec) most animals (9 out of 10) did not learn to discriminate between the two tones in a simple and linear fashion [i.e hold the lever down during the whole duration of S1 and release it (i.e "escape" & avoid pressing) during S2 in acquisition trials] but went through a series of different stages in performance:

- In a first stage, they stopped ("suppressed") lever pressing altogether as soon as the tones were introduced, this happened usually during the first trial block (20-25 reinforcements).

- In a second stage, they learned to ignore the two tones and held the lever beyond the end of the delay regardless of which tone was sounded, this happened during the first and/or the second trial block.

- In a third stage, the animals came to associate S1 with the reinforcement (S2 being still "neutral") and responded to it in a classical manner regardless of its duration. This caused the reinforcement to be cancelled (when S1 lasted less then 1 sec) and led to a slight extinction in some animals and complete extinction in other animals. In the meantime they often held the lever down even after the offset of S2 (this type of performance was termed "Type I discrimination").

- In the fourth stage, the animals learned again to hold the lever down for the whole duration of the 2 sec-delay regardless of which tone was sounded.

- In the fifth and final stage, they eventually learned both the classical and instrumental associations involved in the discrimination task and came to hold the lever down for the whole duration of S1 and release it before the offset of S2, in acquisition trials. (This type of performance was termed “Type II discrimination”).

It was only after 7 to 10 discrimination training sessions of 4 trial blocks each (1 trial block comprising about 25 to 30 reinforced lever presses), that the animals started discriminating successfully. During the course of discrimination training their performance oscillated between type I and type II discriminations, and because of the behavioural constraints already mentioned (The different stages in performance), the strategy used in the second set of experiments was to rely more on the overtraining reversal effect (ORE) than on the serial reversal effect (SRE).

b) Detailed results and discussion:

The results obtained on the second set of experiments showed that:

Behavioural learned changes (behavioural acquisition and reversal) occurred later than neuronal learned changes. That is behavioural conditioning occurred much later than neuronal conditioning. For example, during acquisition trials, lever releases during S2 occurred 250-500 msec after tone onset, whereas multiple unit increases to tone onset had latencies of 12-20 msec. In some cases behavioural reversal occurred after 50 trials, whereas neural reversal occurred after 20 trials.

Multiple units from the BIC and the dorsal part of the midbrain reticular formation showed short latency (<=16 msec) discrimination responses to the tones. Reversal of these responses during reversal training was mainly seen for BIC neurones. Indeed discriminative short latency multiple unit responses and reversal of these responses were found in 3 of the 30 probe tip locations in the BIC and in 1 of the 51 probes in the reticular formation (See Fig 6,7 & 8 in Appendix). In addition to these onset (phasic) responses, there were tonic differential responses from two (02) probes in the ventral reticular formation. Furthermore, it was found that the late responses (>=32 msec) of BIC neurones were not affected by reversal. This would perhaps suggest that early responses (12 to 20 msec) may reflect tonic influence by the reticular formation, whereas late responses reflect sensory characteristics of the stimulus. In support of these late sensory specific responses, Olds(1969) reported that neurones from BIC did not exhibit any associative responses with a 50 msec time-bin duration analysis. However the tonic influence of BIC neurones by reticular formation might itself be secondary to a tonic cortical influence because ventral reticular onset responses showed longer latencies than onset responses of both BIC and dorsal reticular formation. The idea of cortical feedback control of incoming information has been proved to be more valid than Herandez-Peón's (1961) "afferent neuronal habituation" and there has been increasing evidence in support of extra-reticular centrifugal control mechanisms (Desmedt, 1960; Desmedt, 1975; Watanabe et al, 1966).

In opposition to most reports about classically conditioned unit responses, such as those of Olds et al (1978), Disterhoft and Stuart (1977) and Vertes and Miller (1976), it was found that it is the negative stimulus (signalling no reinforcement or RF) that caused greater unit firing (i.e greater neuronal conditioned responses) than the positive stimulus (signalling reinforcement or RF) during our differential operant conditioning experiments.

Indeed, in 38% of all the cases (82% in the case of BIC neurones) multiple units showed greater rates of firing to S_2 than to S_1during acquisition whereas in other experiments (Disterhoft and Stuart,1977; Gabriel at al 1975; Olds et al 1978… etc.) it was found that it was the positive stimulus (CS^+) which caused greater firing.

Greater rates of firing to the negative stimulus could be imputable to either the learning paradigm (operant conditioning here), the physiological characteristics (inhibition to low frequency tones and excitation to high frequency tones) of the area recorded from, or some complex mechanisms mediating inhibitory gating of aversive stimuli.

Moreover this kind of activity was not limited to auditory pathways such as BIC but was also seen in ventral and dorsal parts of midbrain reticular formation. However in the case of the reticular formation, unit responses were non-specific, tonic rather than phasic and could be due to the state of arousal of the animal. It was often seen that during nonreinforced trials, some animals became very active and developed “superstitious” behaviours like excessive drinking between trials (see PART I paragraph 3a).

Nonetheless as the patterns of firing to the tones mentioned above were seen not only during the V.I 90 sec schedule but also during the PR 50% schedule in which the animals were unable to predict the occurrence of either tone, the short latency discriminative multiple units reported here would only be accounted for by associative changes. Whether these changes were local or due to secondary influence from other distant areas still needs to be unequivocally determined.

There are very few studies which reported conditioning and reversal of short-latency (12-16 msec) multiple unit responses from the auditory system of the rat during a differential operant conditioning task.

Long latency (≥ 32 msec) multiple unit responses from the BIC remained unchanged during reversal whereas short-latency (≤ 16 msec) responses reversed suggesting that the latter were the results of associative changes and not due to sensitization, selective orientation to the tones or generalized arousal.

Ventral midbrain reticular neurones seemed to exhibit arousal induced tonic increases to the negative tone whereas dorsal midbrain reticular neurones exhibited mainly phasic responses.

Indeed the results indicated that 9 of the 45 dorsal reticular multiple units and 21 of the 30 BIC multiple units responded with short latency (12-20 msec) increases in firing to S_1 and S_2

and that responses to S_2 were larger than those to S_1. In addition, there seemed to be a constant feature in the pattern of firing of multiple units recorded from the BIC. Namely that early response increases (12-32 msec) were the reverse of late response increases (≥ 32 msec) to the stimuli and that there was no differential responses which could be due to arousal, prior to the presentation of the tones. As to the ventral reticular formation multiple units, 3out of 9 exhibited patterns of firing that reflected both phasic and tonic components : onset responses to the tones had longer latencies (≥ 16 msec) than those of BIC and dorsal reticular formation neurones with responses to S_2 being larger than those to S_1 for both early and late components.

It was also found that in some cases (3 out of 9) and during the V.I 90 sec schedule, dorsal reticular formation neurones unlike ventral reticular formation neurones, fired during acquisition with onset bursts, to S_2 but not to S_1, and in all cases did not exhibit any differential firing prior to these two tones. This would perhaps suggest that the midbrain reticular formation may play a role in the reaction of the animal to aversive situations or stimuli associated with non-reward.

4- General Discussion And Conclusions:

It would not be unreasonable to suppose that because all animals in the present study had been overtrained to get their food by holding the lever down for a duration of 2 seconds, they came to develop strong lever press-reinforcement (LP-RF) expectancies. Thus whenever a lever press was followed by a tone that signalled no reinforcement, there was a greater chance that this stimulus acquired aversive properties associated with frustrative non-reward[1]. This would in turn cause the animal to “escape” such non-reinforced trials. With sufficient training most animals exhibited such behaviour and

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[1] - As well as with Conditioned Emotional Response (CER) effects.

this consisted a behavioural measure of the frustrative and inhibitory effects of the negative stimulus.

Results from the experiments reported in this study have shown very short latency discriminative unit responses which were recorded mainly from the BIC. It was suggested that these responses were associative (learned) rather than due to generalized arousal, sensitization, differential orientation to the tones or to middle ear muscle (MEM) contractions. That the observed multiple unit increases recorded from the BIC were not due to generalized arousal or sensitization was shown by the absence of differential firing prior to the onset of the tones during the V.I 90 schedule and the unchanged late multiple unit responses (latency $\geq$ 32 msec) to this tones during reversal. Differential orientation to the tones as a possible source of differential multiple unit increments was ruled out by the PR 50% schedule experiments.

As to MEM contraction effects on neuronal activity, Møller (1974) reported that they were absent for tones of 1 kHz and 4 kHz in frequency and 75 dB in intensity (the same parameters as those of S_1 and S_2 in this study).

5- Learning Induced Plasticity Of Sensory Systems In The Light Of Recent Studies:

Apart from the pioneering work of Hubel and Wiesel in the beginning of the sixties on sensory system reorganisation during critical periods of development in cats, and the work of Gabriel et al in the middle of the seventies on conditioned neuronal responses in the auditory system of the rabbit, plasticity of sensory systems during learning has long been very much underestimated in research work and experimental studies on the neurobiology of memory and learning, between the middle of the seventies and the end of the nineties. It is only during the last ten or fifteen years that several laboratory studies have reported plasticity phenomena in sensory systems of adult animals induced by learning. Such recent findings have been discussed and reviewed by Edeline, J.M (2002, 2003 & 2004) & confirmed in many occasions by few eminent neurobiologists like Shulz , D.E and his colleagues (1999, 2000, 2001, 2002 & 2004) or workers like Kilgard, M.P & Merzenich, M.M (1998), Tillmann, B (2003) Rauschecker, T.P (1999).

In addition to these new laboratory results it was also found that sensory plasticity induced by learning was at the centre of contextual and state dependent neuromodulation and functional plasticity by emotional, attentional & motivational processes (Shulz, D.E et al, 2000; Ahissar, E et al; 1992 & Shulz, D.E:2002), and that mainly cholinergic neuromodulation (more than dopaminergic or noradrenegic neuromodulations) mediates selective attention, motivation and sensory plasticity (Shulz, D.E et al: 2000 & 2001).

At this point and in support of this new scientific evidence it is noteworthy quoting Jean-Marc Edeline as saying that “since the end of the nineties, several experiments have shown that the receptor field of neurones of the auditory system is selectively modified during learning” and that “these modifications (of the receptor field) observed in the limited period of time of a unitary recording, must be seen as the first manifestations of the reorganization of sensorial maps described in the somesthesic cortex” by other authors (Edeline, J.M: 2002). It is also important to quote at length Shulz, D.E & Shulz, D.E et al as confirming that the “past fifteen years research on the neurological bases of learning and memory have shown interactions between sensorial cortical representation and behavioural learning” that **“the search for neuronal sites of plasticity induced by learning in invertebrates, as well as in mammalian sensory systems has disclosed the involvment of primary levels of**

integration in sensory systems"[1](Shulz,D.E 2002) and that "experimental studies on acetylcholine (Ach) dependent cortical plasticity have shown that Ach is needed for both the induction and the expression of plastic modifications induced by sensory cholinergic pairings" **with Ach dependent plasticity being not correlated to activity dependent plasticity** (Shulz, DE; Ego-Stengel, V and Ahissar, E:2004).

As to the role of the hippocampus (especialy its CA_3 & CA_4 fields)[2] in the modulation of sensory plasticity induced by learning, it is now a well established well documented, and recently corroborated fact that the septo-hippocampal system is involved in pain and novelty detection, stop mechanisms, comparison between expected and actual stimulation (Gray, J.A; 1971) in the link between topographic and episodic memory (Spiers, H.J et al 2001) and in spatial orientation (Berthoz,A,2001 & Martin, Patrick. D; Berthoz,A, 2002 & Weiner, S,I et al, 2002), and that hippocampal Theta (Θ) rhythm, not only inhibits unrewarded behaviour & modulates[3] long term potentiation (LTP) & CA_1-NMDA receptors activation

(Hyman, J.M et al 2003; Roberts, P.D & Bell, C.C, 2002) but also inhibits ascending reticular activating system (ARAS) activation (Gray, J.A; 1975) while mediating selective neural plasticity & memory retrieval (Belloum, M,2003) as well as anti Hebbian phasic ascending sensory reorganization & sensory plasticity (Abott, L.F & Nelson, S.B 2000 & Roberts, P.D & Bell, C.C,2002).

CONCLUSION

In summary we can say that against this background of experimental results and evidence from previous studies and research, and in view of the present knowledge of the anatomy of the descending auditory system, it appears that the cortex and/or the

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[1] - Underlined by us (M.B).

[2] - Which have projections to the septum.

[3] - With a tendency to inhibition.

hippocampus may be a likely source of arousal-related changes and centrifugal influences in the MGN. The mechanism responsible for modulating the activitty of the inferior colliculus is not well known but could have its source in the reticular formation, the cortex or both (in this case reticular activity might be modulated by corticofugal influence in a similar fashion as that described by Sokolov (1963, 1966).

It is however suggested that BIC and perhaps MGN (mainly MGm[1]) neuronal conditioned responses may reflect hippocampal as well as dorsal reticular phasic inhibitory ascending efferent gating as well as competing cortical and ventral reticular descending tonic desynchronization and generalized arousal.

At the same time anatomical evidence from Gacek (1960) of brachial collaterals to the reticular formation on both ascending and descending pathways between cortex-MGN and the inferior colliculus may also suggest that the afferent and efferent influences of the reticular formation subserve different functions in the processing of auditory information. Namely that ascending influences are “phasic” in nature and would account for the emergence of a phasic component in the pattern of firing of dorsal midbrain reticular formation neurones, while descending influences are tonic and would explain the “non-specific” patterns of firing of ventral midbrain reticular neurones.

In the end we think that the mechanisms which are at the origin of the short-latency phasic discriminative unit responses of the BIC, MGm & dorsal reticular formation, the higher rates of unit firing to the negative stimulus in all case, the long-latency tonic discriminative unit responses of the ventral reticular formation, are mechanisms of a two process kind similar to those of Sokolov for the orienting reflex, (1960), those of Gray for the neurological basis of behavioural

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[1] - MGm: Medial subdivision of the MGM.

inhibition (1972) & those of Jouvet for genetic reprogrammation during R.E.M sleep (1974). Moreover, & in view of the most recent studies & findings (of last ten years) on context dependent plasticity of sensory systems during learning, we may conclude that primary sensory pathways can not only exhibit durable plastic changes, but that these plastic changes occur as a result of a phasic ascending reorganization, cholinergic neuromodulation by nucleus basalis (Kilgard, M.P & Merzenich, MM: 1998: Shulz, D.E:2002), and hippocampal centrifugal gating associated with conditioned emotional response (CER) & frutrative non-reward effects, and not as a result of direct tonic non-specific cortico-reticular influences.[1] Therefore memory is not only dependent on perception but perception and memory appear more and more interdependently and cognitively linked functions especially within two-process approach-avoidance discrimination learning tasks and go/no-go task models.

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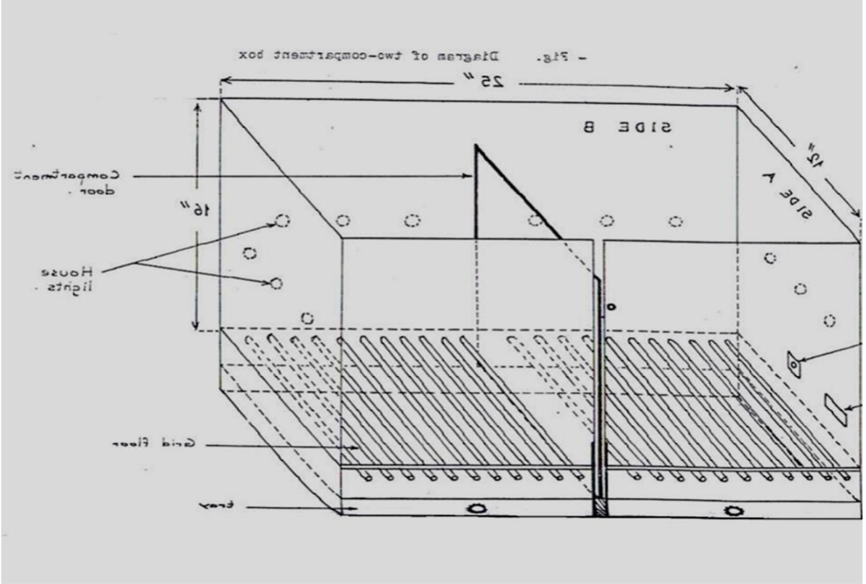
[1] - Or classical Hebbian (synaptic) plasticity.

APPENDIX : Fig 01 to 08



A. The CAP

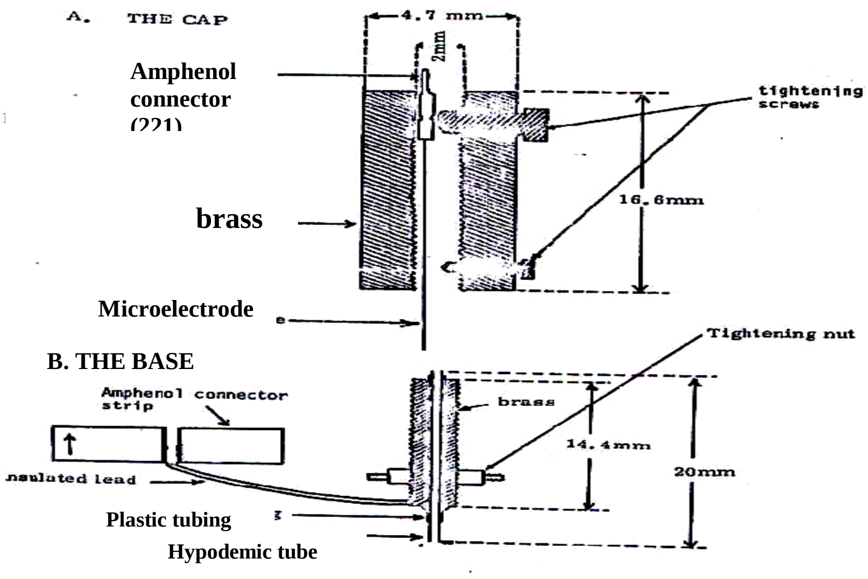


Fig. 2: Moveable micro-electrode assembly (modified from Vertes, 1975).

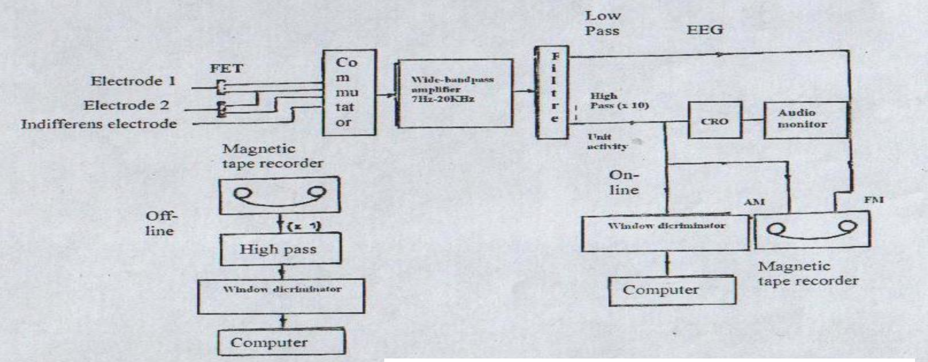


Fig 3 : Information flow diagramme

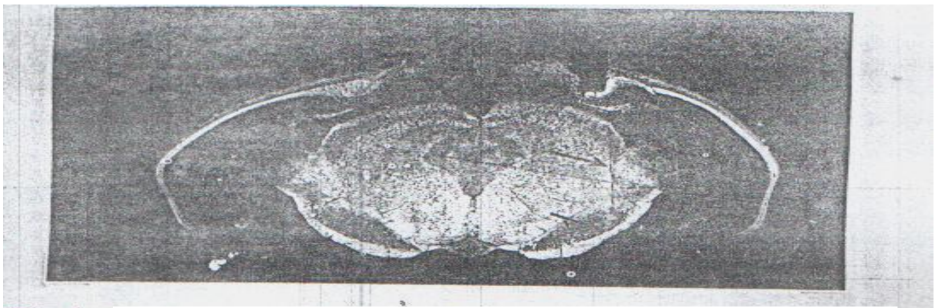


Fig.4a

Histological section from animal P3 showing micro-electrode track going through the brachium of the inferior colliculus (BIC), the reticular formation (RF) and ending in substantia nigra (SNR) (arrows) See konig and klippel Atlas,Fig 49a

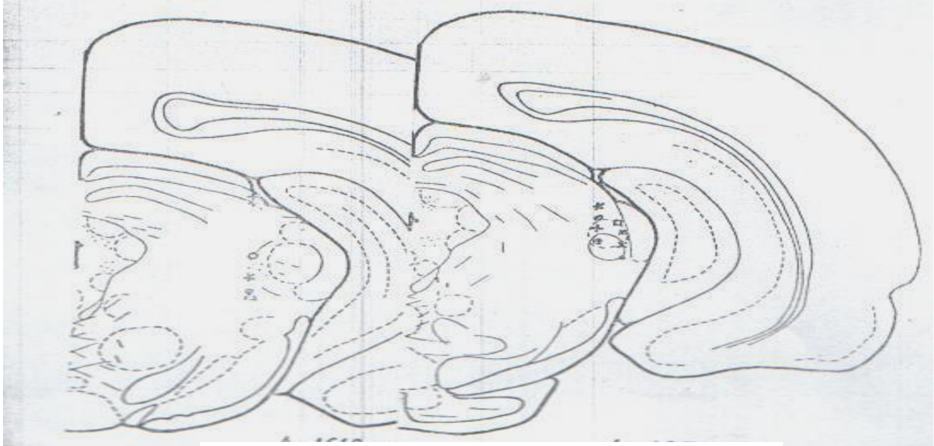


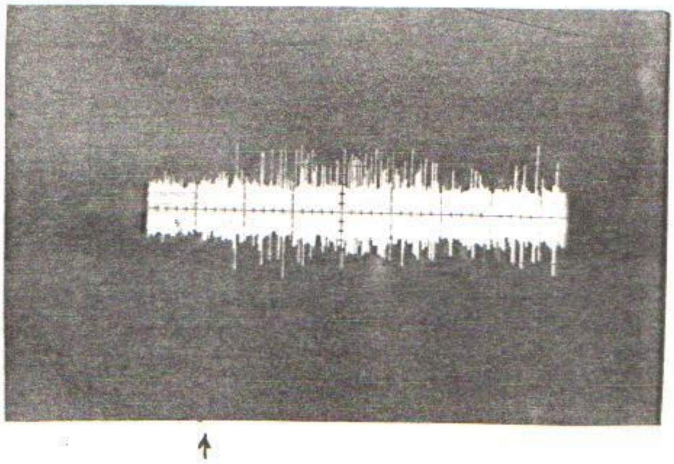
Fig.4b

A 1610 µ **A1270 µ**

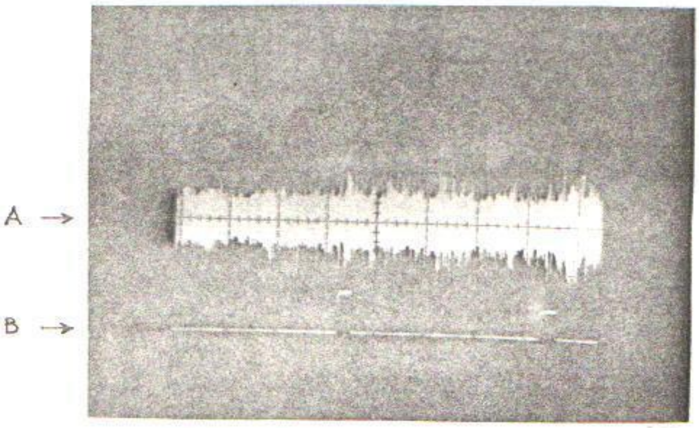
Location of the probes

Fig.5a The figures were reproduced from the konig and klippel Atlas (1963).
A1610µ: ++: MUA P3/5 and MUA P3/6
O:MUA P3/10 *: MUAP3/12
•:MUA P3/13 and MUA P3/14
□ MUA P3/15 and MUA P3/16

A1270µ: *: MUA P4/5 O MUA P4/6
+:MUA P4/7 •: MUAP4/9
□:MUA P5/3 □ MUA P5/4
¤ MUA P5/6 •MUA P5/7

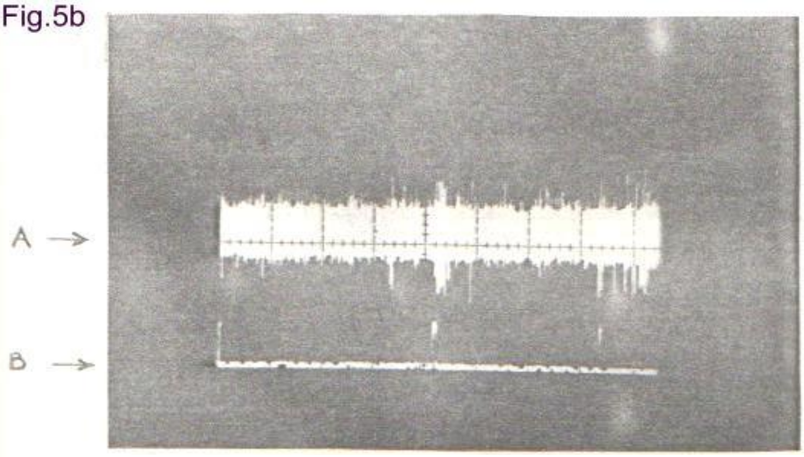


Bun turned off
MUA P3/12 Response to cessation of BUN

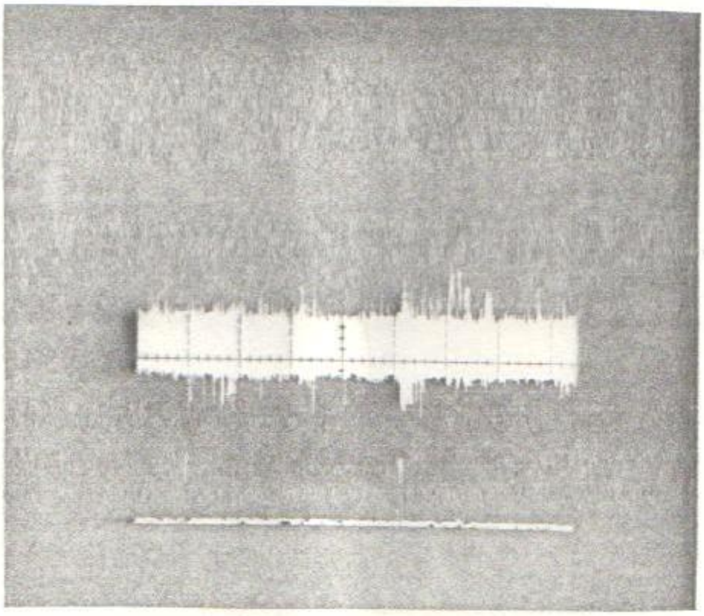


MUA P3/15 Pattern of firing during lever pressing for food with a 2-second delayed RF. (A) : Multiple Unit Trace (B) : Lever press pulse followed by RF pulse . Time base : 0.5 sec/div

Fig.5b



MUA P4/7 Responses to onset and offset of a 20 second – 500 Hz tone (1st tone presentation) (A) Multiple unit trace. (B): Onset pulse followed by offset pulse then 2nd onset pulse time base: 5sec/div



MUA P4/7 Response to onset and offset of a 20 second – 500 Hz tone (2 nd presentation of the tone).

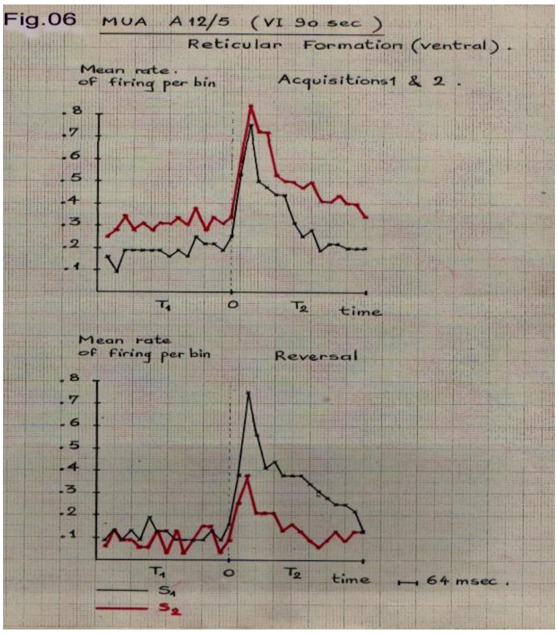


Fig.06 MUA A 12/5 (VI 90 sec) Reticular Formation (ventral).

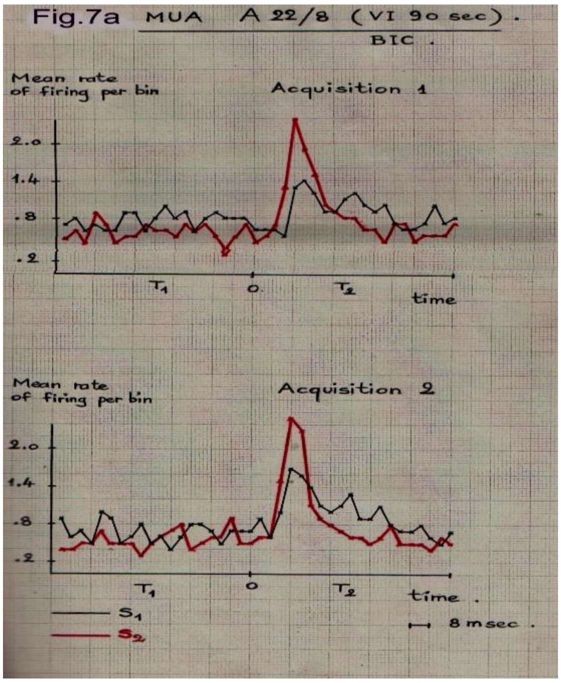
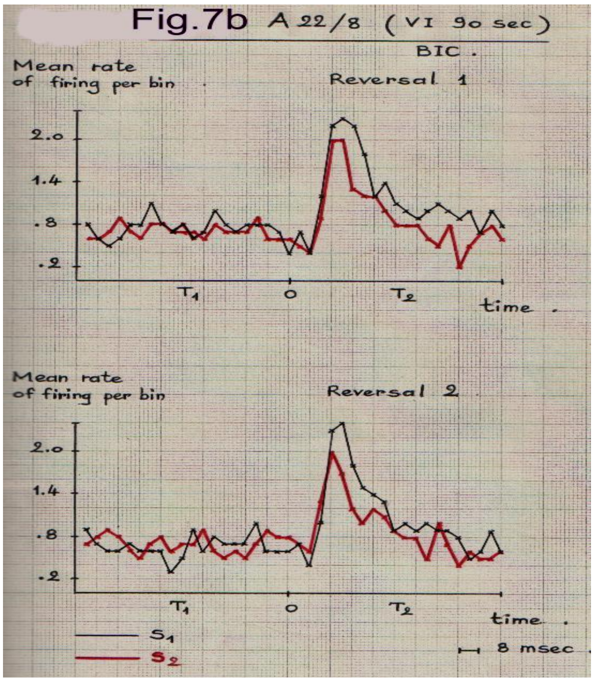


Fig.7a MUA A 22/8 (VI 90 sec). BIC.



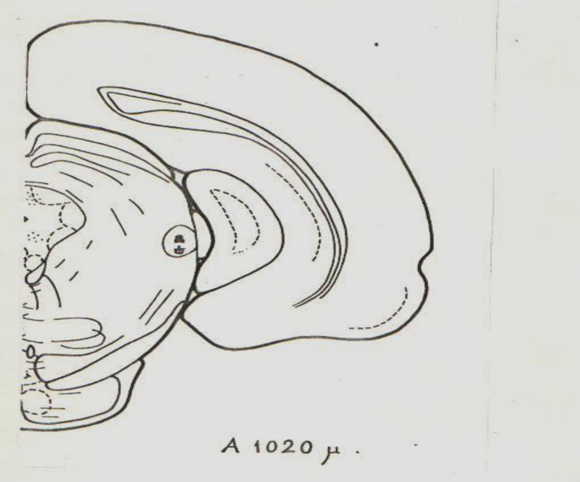


Fig.08

Location of MUA probes (Rat A22):

- ● **MUA A22/3**
- ■ **MUA A22/4**
- \+ **MUA A22/7**
- 0 **MUA A22/8**

The cross – section of the rat brain was retraced from Konig and Klippel (1963)

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