Enclosed are further corrections and references making mine complete through page 440. I will forward the remainder very shortly.

R. W. Sperry

p. 150, line 6: Delete this whole passage: line 6-15 and line 18-19.

p. 152, line 29

SPERRY: There are reports of spinal conditioning in the frog by Franzisket in Rensch's laboratory that seem to be pretty good. In chronic spinal frogs they pair a strong and a weak cutaneous stimulus. The stronger stimulus, to the flank, say, dominates during the conditioning trials and inhibits a response that otherwise would occur to the weaker stimulus, say to the forelimb. (This differs from the usual procedure in which an indifferent or neutral stimulus is used as the conditioning stimulus.) After several hundred pairings, application of the weaker stimulus to the forelimb evokes by itself the flank-wiping reflex of the hind leg instead of the normal forelimb response. The conditioned responses show an early labile phase with a chemical-like waning and a more lasting stable phase after many pairings up to 1500 or more applied over 75 to 100 days.

Rensch and Franzisket (D. 5) appear to have answered the objection that they are dealing merely with temporary heightened excitability and irradiation phenomena. ~~The spinal sections at the base of the medulla were confirmed histologically~~. For some reason they have success with water-frogs but not with some other species.

p. 152, line 35

SPERRY: Before we leave Pavlov, there is one other minor ~~point~~ question. I recall that ~~in Pavlov's lectures~~ he inferred from the cutaneous and auditory conditioning observations, a precise topographic mapping of these sensory fields in the cortex. Is there any possibility that this antedated the direct anatomical and physiological mapping. Does anybody know?

p. 153, line 8

SPERRY: Do you know whether this preceded the more direct anatomical demonstration of the topographical detail?

p. 153

l. 11-12 Delete.

p. 235, line 22

1 SPERRY: If it should be true, as seems likely, that your central stimulation ~~here~~, in order to be effective has to evoke a sensation,-- auditory, visual, or whatever, depending on the area you are in,--then it is possible that~~, with~~ a peripheral stimulus~~, one~~ would ~~have~~ allow better control ~~over~~ of the exact nature and ~~even the~~ intensity of th~~is~~e evoked sensation. ~~than is possible with this method.~~

p. 163, line 15

SPERRY: I don't want to change the subject, but--

p. 163, line 18:

SPERRY: Would you say, Dr. Liddell, that there has been any significant development in the brain theory of conditioning since Pavlov's time?

p. 167, line 17

SPERRY: In thinking back at this point, I'm concerned that we could be leaving an impression that Pavlov's theory has remained the accepted and prevailing physiological explanation of the conditioned response up to the time of the recent implanted electrode studies.

p. 167, line 22

SPERRY: I would have guessed that his conceptions of irradiating excitation and inhibition have been considered ~~quite~~ inadequate for at least twenty years.

p. 167, line 27: Delete lines 27-29.

p. 176, line 17

SPERRY: Has anyone tried to establish these ~~[illegible]~~, visceral-visceral conditioned reflexes in decorticate animals?

p. 185, lines 15-27: Delete.

p. 208, line 6 (continued)

Now that we are approaching the new implanted electrode work, I wonder if it would not be helpful, particularly for those of us not working on conditioning, to summarize briefly some of those conditioning phenomena that have seemed particularly relevant to brain theory. I can start by mentioning a few that come to mind and probably others here can add to the list.

First, I think we have not yet mentioned conditioning under curare. Apparently the process goes perfectly well in the absence of any motor response. The motor response has been eliminated also, I believe, by crushing of the nerves, and further, by local anesthetization of the motor cortex, which, of course, blots out the--[Doty says "No."] Well, you correct me on that.

p. 208, line 35

SPERRY: In any case, there have been experiments in which ablation of the motor cortex has failed to abolish learned responses (E). This should eliminate as a necessary part of the brain mechanism the dominant focus of attraction in the cortex that according to Pavlov was supposed to funnel the conditioning stimulus excitation down into the reflex motor pathways.

The effect of random reinforcement is particularly critical for any brain theory. We estimate the strength of the conditioned reflex in part by its duration and the difficulty of extinguishing it. It has been shown (F) that with an equal number of trials in the conditioning procedure, aperiodic, rather than regular reinforcement produces a CR that is much more difficult to extinguish than is the CR formed with reinforcement at every trial. According to most ~~of the~~ physiological explanations you would expect to get a much stronger connection between the brain centers involved if you pair the unconditioned with the conditioned stimulus on every trial.

The effect of alternate reinforcement and extinction has already been mentioned. If you establish a conditioned response, then extinguish it thoroughly, then reestablish it, and then extinguish it again, it has been found that, after so many repetitions of this, the learned response can be reestablished with a single trial (G). This too has important implications for the underlying brain process.

Just the phenomenon of delayed conditioning is interesting. Generally, the signal stimulus precedes the natural reflex by a short period, from, say, a half second--which is about optimum for the eyelid response in man--on up depending on the situation and species. It is possible to set this signal stimulus as far forward as a half hour or maybe even longer. This poses some nice physiological problems as to the nature of the trace effects of the stimulus and how they operate at the end of the delay. The animal somehow has to hold the effect and to respond at the proper time. It is

~~similar or very close to the so-called~~ one kind of "timing behavior"~~. that Galambos and Morgan refer to in their forthcoming chapter in the 'Handbook'~~.

Even the simple absence of reversed conditioning is something to keep in mind in formulating a brain theory. That is, that the signal stimulus has to precede the reflex that ~~you are going to tie it to~~ it is to be tied to. I wouldn't be surprised if there exists in the vertebrate brain in general some kind of a built-in tendency to perceive 'what-follows-what', 'what-leads-to-what'. Appropriate central nervous adjustment in this respect is fundamental not only to our cause-effect thinking, but to the behavior of all vertebrates from the lowest forms to the highest.

In particular, we should ~~keep in mind~~ not forget the examples of rapid conditioning. In conditioning, we have one problem in the initial acquisition of the conditioned reflex, and another associated with its prolonged retention. Generally it is not easy to distinguish the two because in most laboratory conditioning the time span is great enough so that the acquisition proceeds in part on the basis of traces retained from earlier conditioning trials. However, ~~it is important to remember that~~ a great deal of rapid conditioning and learning can and does occur in a single trial or two, not only in the laboratory but also under natural conditions. ~~In working~~ With human subjects, ~~particularly,~~ it is not difficult to establish a conditioned reflex and ~~then~~ to extinguish it, all within a twenty-minute session. ~~A~~ The point is that a lot of learning and conditioning is so rapid that you don't have to deal with the permanent-type memory traces at all. The establishment of the 'temporary connection' becomes a problem primarily of dynamic reorganization. In time the reorganization becomes consolidated through lasting tissue changes. ~~For~~ It is often convenien~~ce~~t in dealing with the brain process ~~changes~~, ~~we can~~ to separate these two phases of the problem. ~~phenomenon: the reorganization process, and the tissue changes for retention.~~

The effect of electroconvulsive shock is of interest in this regard in that electroconvulsive storms wipe out temporary or recent learning, i.e., of trials made up to a half hour or so before the ECS, but do not eradicate the more permanent trace systems.

p. 211, line 1

SPERRY: Yes.

p. 211, line 12

SPERRY: Yes, it is particularly relevant to the problem of the engram and its nature. Another point here will illustrate the rapid dynamic reorganization occurring independently of trace formation. Experiments with human subjects (A) have shown that a conditioned response that required some 15 to 20 trials to establish under the usual conditions, will be performed on the very first trial with no training when the subjects are given a full understanding of what to expect in the conditioning procedure.

p. 211, line 21

SPERRY: Yes, this was in man. I ~~don't recall~~ believe that we have not discussed motor equivalence as seen in instrumental conditioning. This also is difficult to account for with any theory that postulates the wearing in of connections between CS and CR centers. The observation in this case is that an animal will easily and spontaneously substitute for the conditioned response a quite different response if the situation is changed to demand it, or if the goal is perceived to be more readily achieved thereby. There is, of course, continuous motor readjustment of this kind in the learning of new motor skills.

With respect to decorticate conditioning it is worth noting ~~here~~ that fishes have been reported to show excellent learning and retention after removal of the entire forebrain, and Dr. Arora in our laboratory has recently confirmed this. We find also that a visual discrimination can be retained in fishes after complete section and regeneration of the optic nerve. This shows that the memory traces or engrams are not rigidly nor directly connected to the sensory input channels. There probably is a certain amount of reshuffling of optic fiber connections in the brain as a result of regeneration. We infer that the regenerated fibers get back pretty close to the same cells, but suppose that probably they do not reestablish exactly the same synaptic terminals. Whatever the degree of synaptic rearrangement, it does not disturb reactivation of the engram.

p. 212, line 7

SPERRY: Yes. These are color and also acuity discrimination habits. The findings show not only that memory for the habit is retained, but also that color perception is restored in its original form after regeneration. Accordingly, We must infer the existence of another dimension of specificity ~~among the optic fibers~~ in the optic system associated with color. This presumably is superimposed upon the topical specificity demonstrated earlier and associated with directionality (I). The restored visual acuity also approximates closely that of the normal fish suggesting that most of the severed optic axons must succeed in reestablishing functional connections.

Some of the corpus callosum work that Myers and I (J) did ~~have been doing~~ shows that the memory trace system established with unilateral input is set up not only in one hemisphere, but that there is a duplicate set of traces set up in the opposite hemisphere via the corpus callosum. You can cut out the cortex on the trained side, or section the callosum (J.S) after training, and you find that the memory survives in the opposite hemisphere.

Well there are various other--

p. 212, line 33

SPERRY: I think it is fair to say that so far we know of no irrelevant or external agent that can wipe out ~~the~~ long-established engrams. Temperature changes, magnetic fields, concussion electric currents, drugs and the like are ineffective.

We have nothing as yet, excepting just the normal nerve impulses can put them in and possibly can wipe them out. (This latter remains a question as already indicated, i.e., whether or not impulses can actively wipe out the memory trace.) One may wonder here whether the impulses generated in electroconvulsive shock are not as effective in establishing traces as are impulses generated in organized activity. It is entirely possible that ECS treatment, if repeated frequently enough, does gradually wear blankness and confusion into the brain the traces for which in time begin to compete in stability with all but the long-established engram systems. In this regard I like to picture two factors at work in engram formation: first, a transient disturbance or shift of excitatory threshold that tends to recover within a half hour more or less, and secondly, a metabolic-type factor that is constantly at work and tends to maintain and to reduplicate or freeze the existing threshold ~~status quo~~. A slower process, this latter has little effect over intervals of less than 20 minutes or so. The near perfect replication within the engram structure that is achieved in the metabolic turnover throughout a human lifetime is always a source of amazement and may be indicative of the kind of physico-chemical change ~~structure~~ to look for, ~~in the engram~~. An alternative would be trace systems ~~which~~ like the nucleic acids of the genes, which are said to be subject to little or no metabolic turnover.

A modification of Pavlov's theory has been proposed by Kornorski (K) in which he suggests that stimuli have both a gnostic, high-level effect and a lower affective component, and that the new connections are formed between the gnostic center of the conditioned stimulus and the affective center of the natural reflex. Dr. Liddell has mentioned that no really adequate brain theory has been brought forward to replace Pavlov's. At most we have only some vague thinking about the possible nature and location of the new connections laid down between conditioned stimulus and response centers: i.e. that they must be more complex than the direct transcortical linkages proposed by Pavlov, that they probably involve subcortical centers, and that some kind of reverberatory activity may be important in the earlier stages (L). Some years ago I stuck my neck out to suggest that the conditioned reflex does not necessarily depend upon the establishment of traces or connections of any type between the CS-CR centers. The neural association between conditioned stimulus and response was conceived to be a purely functional one and effected in quite a different way (m)--but this is probably is too long a story to go into now.

Well, briefly, the suggestion is that the engrams support the arousal of a perception or 'expectancy' of what is to come in the conditioning situation. Having learned what to expect, the animal prepares through a 'cerebral facilitory set' to make the appropriate response. The excitations of the conditioning stimulus are routed into the new pathways of the CR not by leftover traces but by an active pattern of facilitation and inhibition imposed on the neural circuits by the transient facilitory set. With this scheme there is no need to search for the 'new connections' established between conditioned stimulus and response centers, as almost universally assumed, because there are none there. There is only an evanescent opening or facilitation of these (preexistent) pathways within the conditioning situation. The permanent traces that lead to arousal of the expectancy and preparatory set may be extremely complex and diffused and are tied not particularly to the specific CS, but to countless stimuli associated with the conditioning experience.

Well, this is probably enough. ~~for now.~~ I am sure others can think of further ~~similar~~ background material and issues relevant to the brain mechanism, i.e. things that it would be well for us to have in the back of our minds as ~~when~~ we begin ~~come~~ to try to interpret ~~consider~~ the new data from the implanted electrode studies.

p. 219, line 15

SPERRY: Dr. Gantt, if you record heart rate and respiratory rate, don't these appear in both instrumental and in classical conditioning, and don't they appear prior to the specific conditioned response, such as salivation or leg flexion?

p. 219, line 32

SPERRY: Yes, and I was thinking here that these early visceral effects may indicate a common basis for both types of conditioning. It may be that the classical is somewhat simpler than the instrumental, because, in the instrumental, the animal has to learn not only what to expect from the signal stimulus, but also what kind of reaction to make to best handle the situation; whereas under the conditions of classical conditioning, the animal needs only to learn what the signal stimulus brings and the anticipatory response comes automatically.

p. 222, line 10

SPERRY: Perhaps it is worth emphasizing that literally thousands of studies have been made since the first demonstration of the conditioned reflex in attempts to solve this seemingly simple phenomenon, and that the thing has turned out to be worse than a Chinese puzzle, the solution to which we still are not even close to, a good half century later. In this short meeting, I suspect we can't hope to achieve an effective encyclopedic coverage but will have to be selective, trying to pick out those things that really bear on the brain problem, and trying especially to point up some of the more critical issues that have come out of the work to date, and on which the implanted electrode data may soon shed new light.

p. 239, lines 32-35: Delete this whole passage.

p. 243, line 25

SPERRY: Is there any chance that the motor stimulus is evoking a somatic sensation, perhaps a tingling of some sort in the paw or leg that is lifted?

p. 243, line 29

SPERRY: So you may be dealing with two sensations in close succession, associated also with the afferent effects of raising of the leg.

p. 245, line 6

SPERRY: There have been reports of 'sensory-sensory' or so-called "sensory preconditioning" in animals. The technique, as I recall, is to pair two stimuli repeatedly and then condition a response to the second one. Afterward it is found that the first of the paired stimuli, that never was used in conditioning the response, will, by itself, evoke the conditioned reflex. In man, as you know, there are numerous studies dealing with the acquisition of mental associations of various kinds some of which closely approach sensory-sensory conditioning. Also it has been shown that by conditioning procedures one can get a signal stimulus to evoke sensory illusions and hallucinations.

p. 248, line 18

SPERRY: This must mean, then, that the cerebellar stimulation you mentioned earlier could have been evoking a sensation independently of feedback from the forced movement.

p. 250, line 5

SPERRY: Dr. Doty, before we leave the subject, another point comes to mind relating to motivation and its general role in conditioning: I believe that the so-called "latent learning" which Dr. Olds referred to earlier is sometimes cited to indicate that motivation may not be necessary for the establishment of new linkages in learning and conditioning. There is also a lot of seemingly unmotivated "incidental" learning that is cited in the same connection as is also sensory-sensory conditioning. As I recall it, there is one school of thought that claims that any two excitation processes occurring contiguously in the brain tend to become associated regardless of any reinforcing reward or motivational value, and another school that believes new linkages are not retained in the absence of some kind of reward which, of course, implies underlying drive and motivation of some kind. As I see it, ~~M~~otivation, operating via high-level positive and negative feedback systems, the basic centers for which are being so nicely delineated in the self-stimulation methods of Dr. Olds and others, constantly directs behavior, unlearned as well as learned. Its obvious importance in conditioning may be ~~only~~ largely an indirect one with respect to the formation and reactivation of the engrams, i.e., it may selectively favor repetition and perseveration of adaptive contiguities as against nonadaptive ones, if you see what I mean. In any case the question is still ~~wide~~ open.

Also open is the related question of whether it is necessary in conditioning that the stimuli employed register centrally as sensation in subjective awareness. This, of course, raises a knotty philosophical issue, but I suspect it is not, as many maintain, a pseudo- nor an unimportant problem, especially now that we are getting closer and closer to the central brain mechanism involved.

p. 269, line 6

SPERRY: It would be an easy control to put in a piece of polyethylene sponge and stimulate it.

p. 269, line 10: Delete this remark.

p. 269, lines 23-35: Delete this whole passage.

p. 269, line 27

SPERRY: Did I understand you correctly to the effect that a locus in the caudate previously neutral was changed into an avoidance locus by conditioning procedure? How long did that alteration survive?

p. 269, lines 30-33: Delete this passage.

p. 290, line 4-5: Delete this passage.

p. 301, line 14

SPERRY: I would object to that, Bob, but go ahead.

p. 301, line 18

SPERRY: Yes, but not between the two response or stimulus points.

p. 301, line 22

SPERRY: That's getting pretty safe, but I think I still object to the possible connotations. But let's go on.

p. 326, lines 20-29: Delete this whole passage.

p. 326, line 31: Delete this remark.

p. 326, line 35: Delete this remark.

p. 327, line 18

SPERRY: Would there be a heart-rate conditioning evident by this time, or a respiratory change?

p. 327, line 22: Delete this remark.

p. 330, line 29: Delete this remark.

p. 331, line 27

SPERRY: Does the normal monkey do any blinking with these flashing lights? Is there a wincing response under these conditions?

p. 331, line 30: Delete this remark.

p. 331, line 33: Delete this remark.

p. 332, line 1

SPERRY: I was not thinking of artifacts, but of some kind of central component of a protective flinching or blinking reaction. Is there no indication of such a response?

p. 332, line 6

SPERRY: I'm wondering about the source of such a rhythm whether it's a purely sensory central effect or involves a more complicated system with perhaps motor and peripheral components.

p. 332, line 10

SPERRY: The 3 to 12/second rhythm.

p. 335, lines 20-23: Delete this remark.

p. 367, line 17

SPERRY: Do you have any guess as to what system is mediating the repetitive response in this case?

p. 370, line 18

SPERRY: Is there any chance that there is some uncontrolled pairing with something like your reaching for a light switch, or something of the kind?

p. 370, line 23

SPERRY: Completely isolated, and no consistent timing that the cat might anticipate?

p. 371, line 13

SPERRY: How did you define that difference between expectancy and conditioned response?

p. 413, line 14

SPERRY: I wish I could remember correctly how I got on that list (laughter); I think that it goes back to a pre-coffee-break presentation--

p. 413, line 19

SPERRY: In thinking back, I believe I was concerned about the distinction that Dr. Olds was making between expectancy and conditioning. I think it's worth a further comment because some of us believe that the formation of an expectancy -- or should I say the neural correlate thereof -- is the basic factor in conditioning. The animal learns what to expect from the signal stimulus in the conditioning set-up. He perceives what follows what, and prepares to respond accordingly. This is important from the theoretical standpoint because it directs your thinking away from the common ~~almost universal~~ assumption that the temporary connections, or engrams, must be laid down in some form between the conditioned stimulus center and the conditioned response center. This is why I objected yesterday to the statement, even in qualified form, that some such connection is what we are looking for.

p. 417, lines 33-35: Delete this remark.

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