ACTA NEUROBIOLOGIAE EXPERIMENTALIS

Acta Neurobiol Exp 2006, 66: 91-97

Konorski and conditional reflexes: A historical summary and an addendum

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Review

Abstract. There have been four major pioneers from Eastern Europe in the neuroscientific study of memory and learning: Pavlov, Bekhterev, Beritashvili and Konorski. The thinking of each evolved with the progress of neuroscientific knowledge throughout the world, and save for Pavlov, each encountered governmental opposition to their views. Among the clues largely overlooked in their examination of conditional reflexes was the fact that the animal appreciates not only its own appetitive state but its immersion in the experimental setting. The latter in itself must require considerable, ongoing neuronal activity to sustain it. There is also the question as to whether "motivation" is an essential feature for the formation of conditional connections; and in cases where it is seemingly absent, as in recognition memory, the processes that underlie the astonishing efficacy of such memory formation remain almost wholly obscure. Finally, it is remarked that the cerebral cortex, as initially supposed, may indeed be the governing locus, even of such simple effects as habituation.

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Key words: conditional reflexes, history, motivation, habituation, memory, laterality

Konorski was the last of the Eastern European "giants" that included Bekhterev, Pavlov and Beritashvili. These four, and their numerous students, have the distinction of bringing associative memory under intense scientific scrutiny.

Pavlov, the most renowned of the group, began with the study of digestion under Heidenhain. However, he was certainly aware that his Russian predecessor, Bubnoff, in the same postdoctoral position as himself, had produced a monumental, and materialistically oriented, study of the brain, using electrical excitation (Bubnoff and Heidenhain 1881). Pavlov's later conceptualizations of brain mechanisms have clear links to this study, both as to the interplay of excitation and inhibition evoked from or within the cerebral cortex, and in his insistence that objective analysis must prevail in assaying these neuronal processes and their mental consequences, despite their obscurity.

Bekhterev also studied in Germany, first working on the superior vestibular nucleus with Flechsig in Leipzig. He also spent some time with Wundt, as well as Meynert, Westphal and Charcot (Lerner et al. 2005; Lerner and Witztum 2005). Thus, unlike Pavlov, Bekhterev was dedicated to studying neural and mental activity from the beginnings of his career. In his volume on "reflexologie" (Bechterew 1926) he notes that in 1885-87 he was training dogs to "give their paw" upon command (Archiv für Psychiatrie, 1886-87). Damaging the corpus striatum abolished this learned response, providing an early, and forgotten, adumbration of the thesis that "habits", such as conditional reflexes, are supported by the basal ganglia (see Mishkin et al. 1984). In their book, that was uniquely prominent in drawing Western attention to conditional reflexes, Hilgard and Marquis (1940) provide a cogent review of the work of Bekhterev vis à vis Pavlov. Aside from his extensive clinical observations, however, Bekhterev's work on association reflexes, as he called them, is far overshadowed by the Pavlovian corpus. While some of this is perhaps attributable to his ambitious (over)extension of the "reflex" idea, and the sparsity of experimental details in his voluminous descriptions and extrapolations, another factor may be the suppression of his work during the Stalinist era. Indeed, there is considerable reason to suspect that Bekhterev was poisoned by the Stalinist police, following his less than prudent public comments that his patient, Stalin, was paranoid (Brackman 2001; Lerner et al. 2005).

Beritashvili (see Doty 1975) was thoroughly trained in neurophysiology, with Rudolf Magnus, and in the 1920s wrote two lengthy reviews on the subject for the Ergebnisse der Physiologie. Concurrently he published a two-part review on conditional reflexes for the journal Brain, "individually acquired" reflexes, as he called them, to distinguish them from innate, genetically developed reflexes. Much of his work was devoted to studying mnemonic capabilities across the vertebrate spectrum, noting particularly the progressive increase in duration and quality of memory from fish to a severely microencephalic girl (Beritashvili 1971). He found differing characteristics for three types of memory, "image driven", "emotional", and "conditional reflex". The latter even in mammals was found to be a function of the entire brain (as per Bechterew 1926, and Mishkin et al. 1984 above; and see Thompson, this volume), that with phylogenetic development migrated to varying degrees from the cerebellum and midbrain to neocortex. Emotional memory is equivalent to one-trial learning of a fear response, increasingly prevalent with development of the forebrain. Most interesting is image memory, which is exemplified by the ability of a mammal to retain memory for the place where food was once encountered, and return to that location days or months after the first experience. The "image", obviously, is an inference, yet it would be obstinately illogical to deny to the animal neocortex the ability to generate a ghostly replay (memory) of the initial event as a guide to subsequent seeking. Thus, Beritashvili calls upon "image units" to subserve this function, somewhat as Konorski does with "gnostic units" to participate in analytical processing.

Among the four, Konorski was the only one not to have direct experience in laboratories of the West, yet he rivaled Beritashvili in his knowledge and use of data available in Western languages. Having worked directly with Pavlov, his interpretations at first relied somewhat upon block diagrams and arrows to represent cortical areas as accounting for the data, and these remained a useful if simplistic didactic tool. However, he also continued to extend analysis in new directions, as initially exemplified in his work with Miller on conditional reflexes in which the animal became an active participant in the process rather than a passive recipient, upon whom the conditional and unconditional stimuli ineluctably descended (see Zielinski, this volume). He and his many students made good use of electrical stimulation, and limited extirpations of vari-

ous neuronal loci, describing their procedures with care, unlike many of the reports of Pavlov and Bekhterev.

It should be noted that, in context of the times, it took more than a modicum of courage to forthrightly embrace findings of Western science, or to obtain results contradictory to Pavlovian dogma. Beritashvili was called before the Academy of Sciences of the USSR to renounce his errors in this regard (Doty 1975), much as Galileo before the Pontificate. Happily, Konorski was one step removed from these dangerous proceedings; yet he, too, lived under the Stalinist sword, and chose largely to ignore it.

Turning now to conditional reflexes per se, there are two intertwining threads that are often ignored in endeavors to relate them to underlying neuronal processes. These are the overall setting of the experiment, that forms an inevitable part of the conditional stimulus, and so, too, does the motivational or appetitive state of the animal. Although I know of no specific tests, it seems highly unlikely that the dog, walking about in its home pen, would salivate upon hearing the tick of the metronome; certainly not if it were well fed. This overriding influence of the experimental chamber was dramatically shown by Giurgea (1986). The experiments were conducted in two different rooms separated by a long corridor. In the morning the dog was trained in room A on a conditional reflex for food, and in the afternoons on a shock avoidance paradigm in room B. After these reflexes were thoroughly established, the behavior of the animal in the corridor leading to these rooms was unequivocal. When being led in the direction of room A, the animal was lively and eager, but when the experimenter reversed course and began leading the animal toward room B, its behavior changed to a cowering reluctance to proceed. Be it image driven behavior, or whatever, it is clear that the animal maintained certain expectancies in relation to these places. The problem is, what ensembles of neurons are discharging to constitute these "states"? Is there a continuing background discharge of neurons that goad "hunger"? In other words, what is the neuronal nature of a "state", and could some continuing firing pattern be found to underlie it?

Within this untidy question of motivation there is also that as to whether "motivation" is an essential requirement for the formation of conditional reflexes. In a series of experiments Giurgea and I (Doty and Giurgea 1961) showed rather convincingly that it is not. Two loci within the cerebral cortex, both of dogs and of macaques, were chosen for brief applications of electrical excitation. The antecedent site was in sensory cortex, while the subsequently excited area lay within the motor sphere and produced movement. Repeated pairing of the antecedent (CS) and subsequent (US) stimuli, at intervals of a few minutes, 6–10 times per day, eventually yielded a response to the CS that imitated components of the movement elicited by the US. In striving to insert a motivational factor into these results, i.e., formation of an entirely new response to the CS, resembling that elicited by the US, others have pointed to such a conditional reflex as being motivated by postural adjustment. This does not hold, however, on several counts, mostly because the conditional reflex was commonly terminated before the unconditional reflex was evoked. Furthermore, the macaque "sat" in a chair, and no significant postural adjustment was required to make the conditional movement of its forearm. More specific, in relation to the question of motivation, was that the animals had no hesitation in pressing a lever that delivered the US and resulting movement, even though presentation of a modest auditory stimulus alone, (no cortical stimulation) concurrent with such a lever press, was sufficient essentially to abolish pressing. These results by no means discount the fact that the emotional state can augment or inhibit the formation of conditional reflexes; but they do show that the essential feature is the temporal concatenation of the two cortical stimuli.

This is another aspect of the formation of conditional reflexes that is consistently overlooked in seeking neuronal explanations of the phenomenon. In the normal course of events it is the subsequent action that is changed by that which precedes it. This is the case with post-tetanic potentiation (PTP), where antecedent action in a set of synapses changes their ionic environment and thus their excitatory state. However, in the formation of conditional reflexes it is the response to the antecedent stimulus that changes. I have called this the "temporal paradox of conditioning" (Doty 1979). Somehow the effect of the subsequent US plays back upon the neuronal circuits of the CS such that the effect of the latter is altered; quite unlike the characteristics noted for PTP, where the synaptic system is enhanced but the nature of the response remains.

As noted by Zieliński (this volume), Konorski proposed that conditional reflexes can be formed only because of pre-existing "potential connections". In a sense, the experiments of Giurgea, just summarized,

suggest that any two, randomly selected sets of cortical elements could be brought into a conditional relation simply consequent to the temporal relation in their discharge, and without motivational reinforcement. The procedure was definitely not very efficient, since a rather large number of trials were required to induce it, and the motivational component in the ordinary course of conditioning considerably augments efficiency. Nevertheless, two problems arise in pursuing the ultimate logic of pre-existing connections that might, without motivational support, become effectively connected. Although there may well be neurons that seldom discharge, electrophysiology consistently reveals desultory background activity seemingly uncorrelated with definable input. There is thus a massive ongoing neuronal activity that has the potential to form multiple, random and nonsensical, "nonmotivated" connections. Presumably, this is a rare or nonexistent occurrence because, lacking such "motivational" support, random concatenations are too weak to survive without consistent repetitions.

Yet the other side of this coin is the ability on a single, brief trial to form permanent connections for image memory, despite the stimulus input that on the occasion activates a unique ensemble of neurons among the essentially infinite number of ensembles possible. All human beings can testify to this phenomenon, the recognized recurrence of activation of that particular ensemble (or elements thereof). The permanence of this one-trial visual recognition memory is astonishing, as Beritashvili (1971) in his experiments with image-driven memory so cogently described. We (Ringo and Doty 1985) found that a macaque, having viewed a large series of colored, complex forms for a total of only 30 s, was able to distinguish these images from a large inventory of highly similar images 6 months later. This is efficiency at an extraordinary level, but where is the motivational input? Clearly, something is different here from the training that may take dozens of trials to organize an enduring ensemble of arbitrarily selected neurons into a conditional reflex. The answer may lie in the possibility that the massive neuronal background activity is not "noise", but an organized filter (consciousness?) against which inputs must compete for significance. The inputs that rise above the background are not only perceived, but undergo the processes of the temporal paradox, their antecedent activity becoming linked with the systems continually recording the "time" (sequence) and place (visual/vestibular recording of position in space). This, indeed, may be what the hippocampus does, providing a special mechanism for promoting these enduring associations between visual inputs and the time and locus of their occurrence, with an efficiency far surpassing that of the mechanism underlying conditional reflexes.

As a final footnote, it should be appreciated that the cerebral cortex is still very much in play, even though the cerebellum, brain stem, basal ganglia, etc, are now recognized as participating in the phenomena of conditional reflexes. This was evident even in such a simple phenomenon as "habituation", the gradual diminution and ultimate disappearance of an elicited behavior when no stimulus or consequence ensues upon the repeated presentation of the stimulus evoking that behavior. The experiment was performed by ňernicki and coauthors (1997) on unanesthetized, pretrigeminal cats. Such preparations were a specialty of ňernicki, and could be kept in good condition for weeks. The pretrigeminal transection precludes pain, and the EEG shows that such animals spend most of their time awake. When aroused, they do respond consistently with an ocular following reflex to upwardly moving bars or objects. When such movement was repeatedly presented in one visual field at 15 s intervals over groups of trials separated by 3 min between sessions, the ocular following movement in 9 cats was completely abolished within an average of 200 trials. The stimulus was then shifted to the other visual field, and the response to upward movement in that visual field was lost within an average of 22 trials for 4 animals. However, in 5 animals in which the corpus callosum had been transected 2 weeks prior to testing, the second visual field required an average of 248 trials before full habituation occurred. In other words, habituation in each visual field of the callosotomized animals was normal, but in the absence of the callosum there was no transfer between hemispheres/visual fields. Thus, for this ocular following, each hemisphere could be habituated independently, despite the simplicity of the reflex and the abundant cross connections in the superior colliculus. Clearly, when the callosum is present, the cortical system of one side transfers the effect of habituation to the other, whereas subcortical connections do not.

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Received 6 March 2006, accepted 21 March 2006

Comment

ON COURAGE, TIMES AND CHALLENGES

I would like to comment some statements by Doty and some Authors commenting the paper of Zielinski (this issue of ANE), to the effect that Miller and Konorski's fundamentally important distinction between classical and instrumental conditioning was a major departure from the Pavlovian dogma of that time and that the challenge of that Soviet dogma must have been very difficult for the young students in the late 1930s, showing their courage and integrity. I would also like to comment Doty's remark that Konorski was removed from the dangerous proceedings that destroyed Bekhterev and hurt Beritashvili when he went in conflict with the Communist system, or rather made a devastating diagnosis of Stalin's mental health. Doty concludes that Konorski "too, lived under the Stalinist sword, and chose largely to ignore it", remarking that at that time it was courageous to learn and incorporate the findings of Western science, or to obtain results contradictory to the Pavlovian dogma.

I believe, that to some extent this may be a confusion of times and places. The historical background of Konorski's achievements is at present somewhat confusing, especially for the Western reader, so I would like to comment on the situation in various times and places Konorski and Miller lived. While fully agreeing with the opinion about the importance of their findings and their courage, I would like to make clear what and when showed the courage.

Miller and Konorski started their career in the pre-war Poland that was strongly anti-Communist. Therefore, it did not take their courage to challenge a dogma only because it was a Communist one. Neither were there any ideological obstacles in learning the Western science.

Pavlov was held in high esteem not only in Soviet Union, but in the international science in general, as his 1904 Nobel Prize testifies. The same was true about Poland. In spite of bad relations, even animosity, between Poland and Soviet Union between the World Wars, Poland was pluralistic enough so hundreds of Soviet books were translated and printed, including scientific books. Pavlov's papers and essays were twice translated to Polish and, as Konorski writes in his autobiography, this is how he learned about Pavlov's experiments and ideas. At that time Polish scientific institutions, including library of the Nencki Institute received original Pavlov's papers freely. As before the WWI the eastern part of Poland belonged to the Tsarist Russia, most of its educated citizen knew Russian very well. This was very much true about Miller who for some time lived in Russia, and to a lesser degree about Konorski, who was sent by his patriotically oriented father to a high school that taught in Polish language (Russian was taught as a foreign language). Bored by the lack of broader perspectives in the lectures they took during their medical studies, these two discovered Pavlov themselves from the books and were freely exploring his ideas from the source papers. And they did it with passion, discussing every detail, to the detriment of their clinical studies.

What testifies for ingeniousness and great courage of these two undergraduate students from the School of Medicine of the Warsaw University was their unaided realization of the importance of Pavlov's experiments and thorough evaluation of his arguments that showed advantages and limitations of his theory, leading to an attempt of challenging the central dogma of the Nobel Prize winner. All they were equipped at the time they decided to check and challenge Pavlov's ideas were their brains, assertiveness, books of Pavlov and very rudimentary experimental apparatus self-made from materials bought for their own money, as the experimental dogs were. Most of the professors that they approached were indifferent to their ideas, but they persisted until they found Jacob Segal, chair of the Department of Psychology at the Free Polish University who agreed to host their experiments. Taking into account Pavlov's status and credibility, it was a challenge few people would dare. It is also very doubtful if any respectable journal would now publish results of such experiments. Yet, the Warsaw Branch of the French Biological Society in Paris accepted and printed their papers in 1927. What more, when Konorski and Miller wrote to Pavlov, he took their results seriously and invited them to his laboratory.

There are also other hints at the extraordinary qualities of those two. A story from Konorski's youth says that he was so shortsighted that he could not see stars. He refused to believe that they exist until he got his first glasses at the age of 7, and then he immediately admitted that he was wrong. I personally remember that in his last years Konorski was always discussing to-the-point, even with people very new to neuroscience and there was always an impression that all that counts for him are facts and their correct interpretations. At the beginning of the WWII Miller, who was reputedly as talented as Konorski, refused to leave Warsaw because there was nobody to care for his senile parents. He had the opportunity to leave with his wife and knew the danger, yet they both stayed and perished, committing suicide when the Warsaw Ghetto was liquidated.

Konorski and Miller, being Polish citizen and guests that were invited to the Laboratory by Pavlov himself, were largely saved the dangers of the king's-court-like intrigues flowering in his lab and from fierce competition of Pavlov's pupils for a higher place in hierarchy, that was totally dependent on Pavlov's approval. Although Pavlov highly appreciated the importance of Konorski and Miller's contribution to the field of conditioned reflexes, he strongly opposed the idea of two types of conditioning, claiming that there is no difference between them. In his autobiography Konorski wrote, that "(Pavlov) was so sensitive about this point that when writing the above-mentioned paper for his journal we simply did not dare to use our own terminology and called type II conditioned reflexes "motor conditioned reflexes" or "conditioned reflexes of the motor analyser." Both of these terms were misleading. It should be noted that this negative attitude of Pavlov toward the specificity of type II conditioned reflexes had a detrimental effect on the development of the study of these reflexes in Russia."

Therefore, even though Konorski and Miller were not competing for the place of "the best Pavlov's pupil", and were there for only a short time (Miller for a few months and Konorski for two years) they had to bend somewhat under the pressure of Pavlov himself. But then they returned to Poland and were not subjected to Pavlov's authority, intrigues around him or ideological interpretations. These years were rather marked by the debate between Konorski and Skinner, who independently developed the idea of two types of conditioned reflexes but named them differently.

Significantly, there was no animosity to Konorski from the side of Soviet authorities during WWII, when Konorski and Lubińska fled the Nazi occupation of Poland in 1939 and received an effective help from the Pavlov's pupils (Pavlov died in 1936) in emigrating from Latvia to Soviet Union. In a short time they were both given laboratories in the Department of Physiology of the Subtropical Biological Station in Sukhumi (then Georgian Soviet Republic) - the famous Primate Research Center. They started there new research on conditioned reflexes but abandoned it after the Nazi invasion of the Soviet Union, when they decided that it is more prudent to help in rehabilitation of soldiers with the injuries of the nervous system. Shortly after the end of WWII, in 1945, they repatriated to Poland and joined the reconstituted Nencki Institute, again having no trouble in developing their ideas and experiments, though the government of Poland was then Communist and dependent on the Soviet Union and Stalin personally.

It was only in 1949, at the session in Leningrad marking the centenary of Pavlov's birth that the orthodox Pavlovism was introduced and decreed in the Soviet Union. Views of several prominent Soviet scientists, like Anokhin, Orbeli and Beritashvili were denounced as anti-Pavlovian and they were removed from their posts. The idea of the "type II conditioning" was denounced as a manifestation of revisionist tendencies and rejected. Konorski was personally blamed as the culprit. The condemnation was aggravated by the fact that after his return to Poland he managed to write and issue in England his book that attempted to describe the phenomena of conditioning in the terms of Western science, as developed by Cajal and Sherrington. In a short time similar session was held in Poland and many scientists presented sharp criticism of Konorski's ideas, demanding his self-criticism in the Soviet style. At that time Konorski really showed his courage, arguing with some statements, politely refusing to revoke his views and generally not giving up in spite of general condemnation. The difference with the Soviet Union was that he was not arrested or removed from his post and could continue his research in spite of political harassment. Such situation lasted till 1955 when Khrushchev started dismantling the Stalinist system. Many of Konorski's critics admitted then that they acted on the Communist Party's orders, not on their convictions and tried to apologize. At the next scientific meeting Konorski was greeted with enthusiastic ovations. Later he was never asked to shape his views according to political demands. Barriers in communicating with the Western scientists were also largely removed.

The second important point is how much courage did it take to combine Pavlov with Cajal and Sherrington. In the pre-war Poland Konorski had chances of learning about the newest developments of the Western neuroscience. Essays of Lord Adrian and Pavlov were issued in the same volume. The Polish school of neurophysiology had its stars – Cybulski and Beck that were pioneers of EEG and excellent neuroanatomist, Maximilian Rose, who collaborated with Vogt's. They worked in Cracow, Lvov and Vilnius respectively, but in Warsaw there were also good basic physiologists, and the laboratories of the Nencki Institute could offer help the beginning scientists. What more, shortly after his returning from Leningrad Konorski met and married Liliana Lubinska who made her PhD with Louis Lapicque at Sorbonne and returned to Warsaw. They were constantly discussing the structure of the nervous system and Konorski admits in his autobiography that she was the person who inspired him to acquire a vast knowledge of the Western neuroscience by studying scientific literature. Even before the WWII he came to the conclusion that the Cajal-Sherrington's and Pavlov's systems are incompatible mainly because they describe the phenomena of excitation and inhibition in the opposing ways and therefore opposing conclusions should be drawn from them. After analyzing literature and his own results, he came to the conclusion that Pavlov was wrong and Sherrington right. That was not only ahead of the other pupils of Pavlov, but also ahead of the ideas of Hebb and far ahead of Skinner. The idea of the book he wrote in 1947 was in his head already in 1939. This shows his ingeniousness and also courage to take the task of charting another white spot. But he did not have to muster his courage to fight political opponents at that time.

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