

Garth J. Thomas, Physiological Psychologist: An Appraisal of His Contributions to Memory Research

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Abstract

This note is a tribute to Garth J. Thomas (1916–2008), late Professor of Brain Research at the University of Rochester, New York. Thomas was an influential psychologist, albeit for his research in learning and memory, as much as for his work as editor of the *Journal of Comparative and Physiological Psychology*. In his studies, he combined experimental lesions with behavioral analyses. He introduced the terms “dispositional” and “representational” to describe the 2 different types of memory function, and emphasized that memory must be studied not only through behavioristic psychology, but also in a molecular and physiological context. Through his experimentation in rodents, Thomas concluded that distinct neural mechanisms underpin dispositional and representational memory. Prompted by Thomas’ remarks on the future evolution of research techniques, we touch upon some ideas on the engram and the glial theory in a modern perspective.

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The year 2016 marked the centennial of the birth of Garth J. Thomas (Fig. 1), experimental psychologist and late Professor of Brain Research at the University of Rochester, New York.

Garth Johnson Thomas was born on September 8, 1916 in Pittsburg, Crawford County, Kansas. He passed away in Rochester, New York, on July 20, 2008, and was interred at the Gerald B.H. Solomon Saratoga National Cemetery in Schuylerville, New York [1].

Thomas earned his Bachelor of Arts degree from Kansas State Teachers College in 1938, and received a Master of Science degree from the University of Kansas in 1940, before going on to receive a Master of Arts degree from Harvard University in 1943. He obtained his PhD in experimental psychology from Harvard in 1948, after completing his thesis under the supervision of S.S. Stevens (1906–1973), Director of the Psycho-Acoustic Laboratory and author of the milestone *Handbook of Experimental Psychology* [2]. At Harvard, Thomas was also influenced by the behaviorist B.F. Skinner (1904–1990), who was a William James Lecturer at the time (1947–1948), subsequently becoming Edgar Pierce Professor of Psychology (1948–1974) [3]. During World War II Thomas’ graduate studies were interrupted by his service in the US Army Air Corps as First Lieutenant; his wife of 63 years, Mona Gee

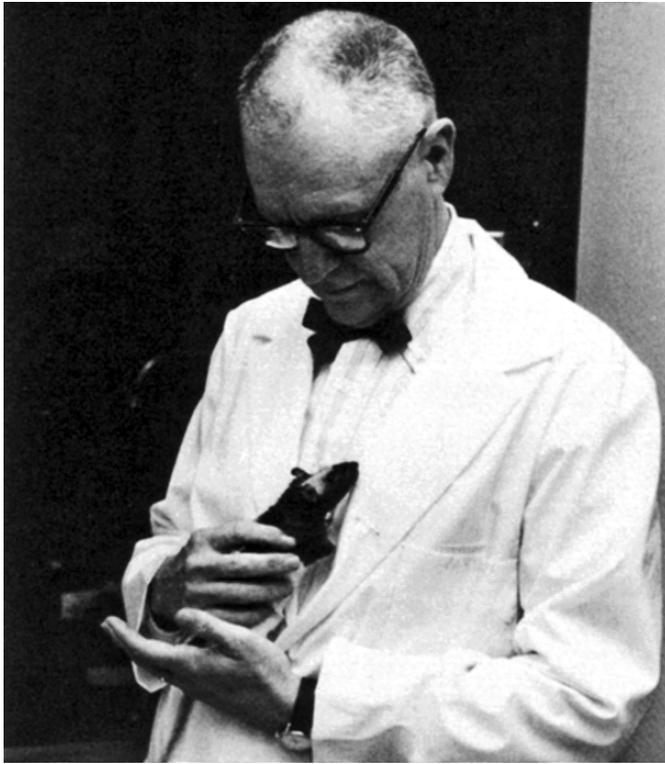


Fig. 1. Professor Garth J. Thomas observing a Brattleboro rat in his neuropsychological laboratory at the Center for Brain Research, University of Rochester School of Medicine and Dentistry, circa 1980. Source: Thomas [10].

Thomas (1920–2012), had also served in the US Army during the War as a psychiatric nurse. In his first publication, still as a doctoral candidate, Thomas and his colleagues investigated auditory afterimages, asking whether they are cases of hearing loss in a specific frequency range or an aftereffect of a previous auditory stimulus [4].

From 1948 to 1954, Thomas was Assistant Professor of Psychology at the University of Chicago, overlapping with R.W. Sperry (1913–1994) [5]. Thomas described Sperry as a “quiet fellow, plenty smart” [6]. He had known Sperry since their Harvard years, and was aware of Sperry’s split-brain experiments in cats. During his time in Chicago, Thomas published a series of articles on psychoacoustics [7, 8]. In 1954, he was appointed Assistant Professor of Physiology and Biophysics at the Neuropsychiatric Institute of the University of Illinois College of Medicine, where he worked for a dozen years. Writing on visual and other forms of sensory perception, he emphasized the need to gain a deeper insight into the visual system beyond the behavioristic perspective [9].

In 1966, Thomas moved to the University of Rochester as Professor of Psychology and Chairman of the newly established Center for Brain Research (CBR), one of the earliest interdisciplinary neuroscience departments in the country with international renown. In the early 1980s, while one of us (L.C.T.) was a graduate student there, the CBR was staffed – besides Thomas in neuropsychology – by Robert W. Doty (1920–2011) in neurophysiology; Leo G. Aboud (1922–1998) in neurochemistry; Manuel del Cerro in neuroanatomy; Ludwig A. Sternberger in immunocytochemistry; and Robert J. Joynt (1925–2012), David Goldblatt (1930–2007), and Robert M. Herndon in clinical neurology, among others.

Thomas taught the graduate courses *Advanced Neuropsychology* (CBR 542) and *Neuropsychological Laboratory* (CBR 541) with the following scope: “the overall goal is to teach students that the function of the brain as exemplified in behavior is their ultimate problem, and that work on all of the neural science disciplines must ultimately relate to behavior. Students are required to plan and carry out a behavioral experiment including collection and analysis of the data and discussion of the results.” His laboratory activities centered on the following theme: “research in general is concerned with brain-behavior relations, especially as regards complex behaviors in which, presumptively, the organism’s behavior is mediated by a brain-constructed stimulus (a cognition, as denoted by some experimental psychologists). Currently and specifically this involves research to elucidate brain mechanisms that mediate alternation behavior” [10].

A gentleman of the old school and a proponent of behavior quantification, Thomas refused to grade his graduate students on a quantitative scale, instead adopting the Satisfactory/Fail option. As Professor Emeritus, after his retirement, he continued to study the behavioral effects of central nervous system lesions on animal memory and spatial behavior. He served on advisory panels for the National Institute of Mental Health and the National Science Foundation, and was elected a Fellow of the American Psychological Association.

Thomas also served as editor of American Psychological Association’s *Journal of Comparative and Physiological Psychology* from 1970 until 1982. Starting in 1974, that journal shifted its focus from behavioral papers, which largely addressed matters of conditioning or learning theory, to behavior studies that included comparative, developmental, evolutionary, ecological, and genetic aspects of behavior, as well as papers that were explicitly comparative in their central thrust, that is, “papers in which the species themselves were chosen for theoretically signifi-

cant and valid comparative reasons” [11, 12]. Emphasis was placed on experimental over strictly observational studies of behavior, and on anatomical-physiological correlates. On the editors’ role, he wrote: “significance is fairly nonobjective and judgmental; what is one person’s significance is another person’s trivia. I know of no solution to the problem of the “tyranny of editors,” but their terms are finite and most are aware of the problem. They do not want to go down in history with the dubious distinction of having rejected Einstein’s first paper on relativity theory, or the like. Most editors are sensitive to the problem of distinguishing significant novelty in science from mere incompetence” [13]. On another occasion, he added: “anything really novel is likely to be given a hard time in the publication process... It is difficult to discriminate truly novel advances in science from inadequate research. If the editor is too accepting, the journal gets to be a vanity press, and it fills with trash... On the other hand, if the editor is too conservative and cautious, the journal might reject the first paper describing taste-aversion learning” [14]. Thomas [14] suggested “that all departments granting PhDs require students to take a seminar in critique writing. Perhaps when the students get out into the world and are asked to review a paper for a journal, they will tend to give more cogent and compelling reasons for their administrative recommendation of acceptance or rejection.”

Thomas devoted much of his career to the study of memory and learning mechanisms, trying to understand these abstract mental processes at a neural level. He reasoned that the attempt to explain memory in physico-chemical terms is a rather difficult task; that is why, most of the time in the past, a dualistic approach had prevailed, implicating “a ghost in the machine.” Thomas claimed that, “as methods and techniques evolve, scientists ought to combat any remnants of metaphysical dualism and animistic explanations,” and argued that “behavioral analysis can establish what an organism can remember under various circumstances, but only physiological events, primarily in the brain as the operator of the effectors and mediator of sensory inputs, can establish how mnemonic processes are accomplished” [15, 16].

In a series of experimental studies, spanning over 4 decades, Thomas dissected the contribution of anatomical areas and pathways, including the precommissural fornix, septal region, septohippocampal circuitry, medio-dorsal thalamus, and prelimbic cortex, to short-term spatial memory, by evaluating the effect of stereotaxic lesions with tests of reinforced alternation in a T-maze [17–22].

We commonly differentiate memory into short- and long-term, with the latter further subdivided into explicit and implicit. Thomas proposed another classification, into “dispositional” and “representational” memory [15, 16]. Dispositional memory is defined as the type that can be accessed unconsciously and includes motor learning, habits, and conditioning; the term is used in the same way as we use the terms procedural or nondeclarative memory today. Representational memory is defined as the type of memory that requires a form of delayed conditional discrimination at the time of choice; in other words, the non-automatic memory that necessitates some trace from the past (images, representations, and so on) as a reference in order to choose the proper reaction. For example, a mouse in a T-maze recalls a former memory for the same pathway to find the way out, using representational memory.

In essence, dispositional and representational memories are not 2 alternate models of memory; rather, they can be viewed as complementing each other. Psychologists mainly tend to use these terms to differentiate our ways of learning [23].

Thomas conducted several studies by experimentally destroying the hippocampal gyrus and its pathways. The posterodorsal septum was selected in particular because of the role of the septohippocampal projection pathway in memory functions. Representational memory tasks were very sensitive to the lesions, as rats were unable to remember their trial-specific learning no matter how much training they had gone through. On the other hand, their dispositional memory seemed unaffected, as they could still remember the behavioral significance of the discriminative cues in the maze [24–26]. Another approach that Thomas pursued was hippocampectomy, which led to distinct results for the 2 types of memory: Thomas and Gash [27–29] observed that hippocampectomy had disastrous effects on representational memory, whereas dispositional memory was only temporarily affected.

Through speculation, and based on Marr [30] proposed model of hippocampus-dependent memory, according to which episodic memories are transferred after acquisition from the hippocampus to the neocortex for long-term storage, Thomas and Ordy [16] concluded that, while hippocampal formation has a “bottleneck,” through which all sensory information must pass in order to become representational memories, such a bottleneck does not exist when one deals with dispositional memories. He reinforced his view by adding that there are extensive connections between the hippocampus and the

sensory and multimodal association cortex in nonhuman primates [16, 27, 28, 31].

Using electrical stimulation with electrodes implanted into deep brain sites, Thomas [32, 33] and Thomas and Stewart [34] had found, from the sequential distribution of responses to several frequencies, that nonspecified brain structures have systems that contribute to the function of learning and display stimulus-induced shifts in background or resting electrical activity, possibly representing functional engrams.

By the time that Thomas wrote his review on the “Neurophysiology of Learning” [35], no systematic research had been carried out to elucidate the specific neural mechanisms of learning processes. The engram existed only as a speculation, as well as in anatomical theories, such as those of Hebb [36] and Konorski [37]. Thus, Thomas focused on studies dealing with neuroanatomical alterations dependent on the acquisition and retention of learned responses. Jerzy Konorski’s theories were largely based on behavioral experiments [37]: he had developed a theory of habituation [38] according to which a targeting reflex occurs to a stimulus in the form of adjustments of the peripheral and central components of the analyzers and an inhibitory reflex occurs to a repetitive stimulus with the latter leading to a suppression of the stimulus input. This theory was, in many ways, analogous to Sokolov’s [39] stimulus-model comparator theory. Sokolov [40] had suggested that there is an internal representation in the brain to which external stimuli are compared; those that are mismatched evoke a response, whereas those that are matched lead to a lessened response. Wagner [41] elaborated on Konorski’s notion, placing greater emphasis on the role of short-term memory and the existing associative network [42].

Today, our understanding of the engram remains incomplete. However, the theory of Semon [43] has received support from modern studies. Learning induces persistent physical and chemical changes in engram cells; moreover, their reactivation results in the retrieval of a specific memory. It is now possible to identify engram cells in optogenetic experiments [44]. Engram cells are characterized by modifications of synaptic strength, the insertion of α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors, a high spontaneous excitatory postsynaptic current frequency and amplitude, and an increased density of dendritic spines [45]. Morphological changes have also been observed at the level of the synapse: long-term potentiation results in the formation of new dendritic spines. In addition to spines being formed and receding, their shape is also modified during

learning events [46] – a theoretical concept credited to Francis H.C. Crick (1916–2004) by Poo et al. [47].

Thomas [35] also discussed other theories of learning, including the theory of protein molecules presented by Katz and Halstead [48], as well as the role of glia. Protein molecules were hypothesized to stimulate the engram, and information could be stored in neurons through excitation-induced specificity of ribonucleic acid molecules that would control the release of neurotransmitters to the postsynaptic membrane, whereas the glial theory suggested that astrocytes may play a substantial role in overall brain function, and, particularly, in long-term memory. The glial theory is still of interest, as it is linked to both long-term and working memories. A mechanism within glial cells appears to sort information for learning tasks; the delivery function of information through neurons render glial cells “the guardians of our learning and memory processes, orchestrating the transmission of information for optimal brain function” [49]. Han et al. [50] further strengthened the view that astrocytes participate in working memory; after removing cannabinoid receptors – proteins that respond to tetrahydrocannabinol – from neurons in mice, they concluded that glia could play a key role in conscious thought.

Through ablation studies, the “localization of function” had been tested in the past. This concept was prone to misinterpretations associated with the discredited theory of phrenology. Thomas tried to understand how lesions affect the brain by analyzing which functions remained unaltered and what changes occurred in the animal’s behavior. Thus, he tested distinctly visual, tactile, auditory, and gustatory senses in terms of discrimination, acquisition, retention, and relearning. Experiments involved neocortical lesions, sensory feedback and conditioned responses, limbic system ablations, interhemispheric transfer, subcortical lesions, conditioning, and interoceptive conditioning [31, 51–53].

He reported that “rhinencephalic” ablations were associated with recent memory loss, and sometimes amnesia and confabulation, and that the limbic cortex seemed to play a role in the inhibitory modulation of motor responses [54, 55]. By developing a within-subject test of spatial working memory and performance in a T-maze based on a delayed alternation, and by comparing the effects of age, of basal forebrain, medial septal, and amygdala lesions, of vessel occlusion, and of drug effects, Ordy et al. [56] provided evidence to conclude that the hippocampus, and particularly the CA1 field, plays a critical role in spatial working memory.

In later studies, ibotenic acid lesions into the paraventricular nucleus of the rat hypothalamus altered behavioral performance via interactions with physiological systems governing arousal level [57]. Three decades earlier, Thomas [35] had foreseen that learning could be understood only through the study of functions, such as instinctive and motor acts, or motivation and affective parameters. The research methods available at the time of Thomas' work were elaborate; he had expressed the hope that, in the future, with the evolution of technology, automatic devices would become available to make the appropriate measurements.

There are still many unknowns in the edifice of memory as a whole. Clinical studies may clarify the blocks of its architecture. An assumption that needs to be experimentally confirmed is whether neurogenesis in the adult hippocampus is linked to the formation of new memories. In that context, Alvarez et al. [58] showed how experience affects the incorporation of adult-born granule cells into the neuronal circuitry of the hippocampal dentate gyrus: the new neurons grow larger dendrites, form more spinous synapses, and become functionally integrated via the chemogenetic stimulation of parvalbumin

γ -aminobutyric acid-releasing interneurons and a disinhibitory feedback loop, when mice are placed in a sensorily enriched environment.

Ongoing research provides new insights into the formation of memories in engram cells of the prefrontal cortex simultaneously with the hippocampal formation [59]. With regard to associative emotional learning, it appears that neurons of the basolateral amygdala are recruited during learning, and become reactivated during memory retrieval [60].

The scientific heritage of Garth Thomas, and his endeavors to understand the brain's mechanisms of learning and remembering things, may provide useful insights for future researchers delving into memory function and its neural underpinnings at the molecular, physiological and integrative levels, aided by the powerful techniques emerging in neuroscience.

Disclosure Statement

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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