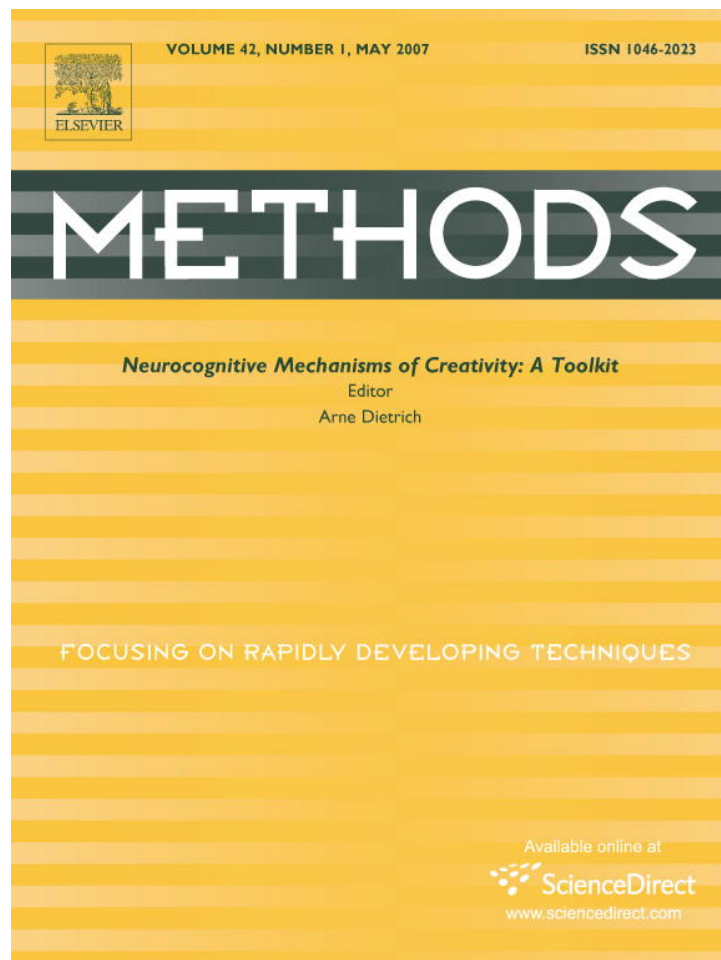


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# Approaches to the study of higher cognitive functions related to creativity in nonhuman animals <sup>☆</sup>

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## Abstract

Fundamental to creativity is prior knowledge and learning capability. One can be creative only to the extent that one's prior knowledge and learning abilities enable. Many of the mental functions of humans that are affected by neuropathology involve levels of learning ability that supercede those used by most animal researchers. Yet there is literature showing that there are similarities in structure and function in the cerebrum within class *Mammalia* and that nonhuman animals are capable of higher levels of learning than those typically studied by neuroscientists. Reviews of abstracts from the 2005 meeting of the Society for Neuroscience reveal that most neurobehavioral research with animals has involved relatively low levels of learning ability. Thomas's [R.K. Thomas, *Brain, Behav. Evol.* 17 (1980) 452–474.] hierarchy of learning abilities has been revised here to better include Learning Set Formation which is fundamental to most forms of higher learning. This paper summarizes both the rationale and the methodologies that might be used to assess the roles of neuroanatomical structures involved in the psychological processes that serve as the bases of creativity.

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## 1. Introduction

Building on prior work by Gagné [1] and Bourne [2], Thomas [3,4] synthesized a hierarchy of eight types of learning. Thomas argued that the newly synthesized hierarchy included Gagné's hierarchy and followed Gagné in proposing that there is no example of learning ability in the animal kingdom that cannot be reduced to one of or combinations of the eight types of learning. Thomas further proposed that the basic types of learning may be used in combinations, either serially, in parallel, or both. Behavioral substrates of “intelligence” and/or “cognition” are

usually based on learning ability. Thus, the hierarchy of learning types is highly relevant for assessments of intelligence and/or cognition. Thomas [4] additionally proposed that it is feasible to adapt any measure of learning ability to different species in ways that minimize the confounding effects of species' differences in sensory or motor capabilities, and/or motivational differences, which may affect *performances* and obscure learning *ability*.

How does such a learning/intelligence/cognition hierarchy (hereafter LICH; to be described in detail below) relate to “creativity?” First, creativity is an abstraction and is not a physical entity, process, or product. Creativity is an abstract concept that may be used to summarize and relate certain observable antecedent events (usually referred to as “stimuli”, “causes”, or in the case of experiments, “independent variables”) with certain observable consequent events (usually referred to as “responses”, “effects”, or “dependent variables”). We cannot observe “creativity” *per se*. We may

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observe certain antecedent events that were correlated with or led to certain consequent events which we may then describe as being a creative act or product. A defining aspect of a creative act or product is that something *new* that is functional in some way has resulted.

Creative acts or products do not occur in a vacuum; they depend on the knowledge and abilities that the creative animal or person is able to apply. For example, a creative animal, artist, musician, writer, or scientist must first acquire certain basic knowledge and skills. Creative organisms can only manifest creative acts or products in relation to what they have learned already or are capable of learning. Thus, for example, a person or animal whose learning abilities are limited to those at the lower five levels of the LICH will be limited to creative acts or products that can be produced based only on those levels of learning abilities. A person capable of all eight levels in the LICH may be able to produce creative acts or products that depend on using all eight levels of learning capabilities.

Many examples can be cited of creative acts by nonhuman animals. Perhaps, the clearest and most pervasive example is that of tool use by animals. One of the earliest scientific reports was by Kawamura [5]. Japanese monkeys on Koshima Island were provisioned by humans who deposited sweet potatoes and wheat grains on the sandy beach. Eventually the monkeys learned to use pools of water to wash the sand from the sweet potatoes and to float the wheat grains thereby separating the wheat from the sand; both were creative acts that became socially propagated among the troop of monkeys. More recently, researchers such as Fragaszy and colleagues [6,7] have studied the acquisition of tool use under laboratory controlled conditions. Other recent examples of creative acts by animals may be found in Wasserman and Zentall [8].

Among the most important implications of the LICH is its application to animal models that better enable one to generalize findings to humans. Two examples where better animal models are needed are (a) to understand the neural bases of human cognitive deficits and (b) to conduct pharmacological research to identify drugs for treatment of human cognitive impairment such as that associated with Alzheimer's disease.

## 2. Overview of the learning/intelligence/cognition hierarchy (LICH)

The eight types of learning form a hierarchy because lower levels, generally, are prerequisites for higher levels (see Table 1). Prerequisite status may be debatable in some relatively minor instances (namely, whether level 2 is a prerequisite for level 3 versus whether they are parallel and whether level 4 is prerequisite for 5 or whether they are parallel). Otherwise, prerequisite status among levels is clear, especially, with levels 5 through 8 where the present emphasis will be. It is important to iterate that learning by most vertebrates is likely to involve the concurrent use of all the types of learning ability in an

Table 1  
A Hierarchy<sup>a</sup> of learning/intellective/cognitive abilities that encompasses all learning abilities evident in any animal including humans<sup>b</sup>

Level 1—habituation OR sensitization
Level 2—signal learning (classical or Pavlovian conditioning)
Level 3—Stimulus–Response Learning (instrumental or operant conditioning)
Level 4—chaining (learning sequences of Stimulus–Response Learning units)
Level 5—Multiple Discrimination Learning: Concurrent Discrimination Learning (CDL) OR Learning Set Formation (LS)
Level 6—absolute and relative class concept learning
Level 7—using class concepts in conjunctive, disjunctive or conditional relationships
Level 8—using class concepts in biconditional relationships

<sup>a</sup> Generally, lower levels are prerequisites for higher levels (see text).

<sup>b</sup> For additional considerations see Thomas [4,5].

animal's repertoire and that such use may occur serially and/or in parallel.

At Level 1 in the LICH, the most basic types of learning ability, are *habituation* and its complementary process, *sensitization*. Domjan [9] defined habituation effect as “A progressive decrease in the vigor of an elicited response that may occur with repeated presentations of the eliciting stimulus” (p. 206) and sensitization as “An increase in the vigor of elicited behavior that may result from repeated presentations of the eliciting stimulus.” (p. 211). The emphasis here is on habituation because sensitization is rarely studied and is of little consequence for present purposes. Habituation has been used extensively with protozoa [10] and habituation has been described as being one of the “...primary behavioral tools used to assess... cognitive competence in early [human] infancy” [11, p. 1352].

Level 2 in the LICH is *Signal Learning* (Gagné's term) [1], a label that Thomas [4] adopted which is, perhaps, better known as classical or Pavlovian conditioning. Level 3, *Stimulus–Response Learning* (again Gagné's term adopted by Thomas) is, perhaps, best known as simple instrumental or operant conditioning. The most defensible distinction between Signal Learning and Stimulus–Response Learning appears to be *who controls the delivery of reinforcement*, namely, the experimenter in Signal Learning and the subject in Stimulus–Response Learning. These two learning processes should be well known and need no elaboration here, as they have been the most studied forms of animal learning [12]. However, other than their prerequisite involvement with higher types of learning they are of less importance in human learning of a higher order nature. Of course, these lower levels of learning are highly involved in the origins and behavioral responses perceived as challenges or stressor in such psychiatric maladjustments such as post-traumatic stress disorder, the various anxiety disorders, depression, etc. These issues and their links to learning are not addressed here. These levels of learning also do not provide the best animal models for the study of human learning at the higher levels of cognition. Level 4,

*Chaining*, involves learning a series of Stimulus–Response Learning units.

Level 5, which Gagné [1] named *Discrimination Learning*, involved learning multiple Stimulus–Response Learning units in parallel. Thomas [3] renamed it *Concurrent Discrimination Learning* (CDL) as being more descriptive of what Gagné meant. However, neither Gagné nor Thomas considered the place for learning set formation (LS). After years of indecision about where to classify LS, it has now been decided that CDL and LS are relatively independent processes that might be subsumed under the more accurately descriptive name, *Multiple Discrimination Learning*; “Multiple” is necessary as lower levels may involve simple discrimination learning.

All classes of vertebrates, except possibly amphibians which appear not to have been tested, are capable of some degree of success on CDL tasks [13]. For example, horses and elephants learned 20 pairs of visual discriminations concurrently. Although rats succeeded in learning only eight visual discriminations, rats are at a significant disadvantage when vision-based tasks are used. Rats were also vastly inferior on LS when vision-based tasks were used [14] but when olfactory-based LS tasks were used, rats performed as well as nonhuman primates [14,15]. It might be that rats would perform as well as horses and elephants on the CDL task, if olfactory discriminanda are used.

In any case, LS [16–18] has been studied far more extensively than CDL, and LS is associated more with an important kind of cognitive processing used by humans. Therefore, LS deserves more attention in animal modeling of human cognitive processes. Preceding Harlow, Bateson [19], who clearly discussed LS but instead used the term “deutero-learning” (second-order learning), applied it exclusively to human endeavors and questioned whether it could be studied experimentally. Harlow showed that LS could be studied experimentally using nonhuman primates, and, subsequently, it has been shown that other mammals, including rats, are capable of LS. Both Bateson and Harlow described the process as “learning to learn” with the implication that the LS (or deutero-learning) experiences facilitate future learning. The view and the evidence is that learning one thing facilitates learning other things, especially when they are related. For example, learning to count facilitates learning arithmetic, learning arithmetic facilitates learning algebra, learning algebra facilitates learning geometry, etc.

It will be useful to summarize how LS *typically* has been studied, but other procedures may be used [17,18]. Typically, an animal is shown two discriminable objects, one of which is predetermined by the experimenter to be associated with a food reward; the same two objects are usually presented for six trials after which a new pair of objects is administered, etc. Prior to its first response, the animal has no knowledge upon which to base a choice between the objects, thus, its first response is made by chance and whether it is rewarded is determined by chance. To be successful over many such problems, the animal must learn

that trial 1 informs which object is correct. Optimal performance on the remaining 5 trials would be to “stay” with that object if the first trial response was rewarded or to “shift” to the other object if the object chosen on the first trial was not rewarded. Levine [20] described this as using a “win-stay”, lose-shift hypothesis.

Harlow [17] wrote “...insightful learning through LS formation is a generalized principle... (that) appears in... oddity learning... (and in)... all concepts... evolve only from LS formation” (p. 510). However, Thomas and his students [14,15] using rats, showed strong acquisition of LS using a procedure that might have, but did not, lead to evidence that rats had acquired the oddity concept. Nevertheless, what seems to be unquestionable are (a) that, as Harlow and Bateson have defined and applied it, LS is a process that might facilitate both class and relational concept acquisition; see below, and (b) that LS is a higher order form of learning than those encompassed by levels 1–4 of the LICH.

LS involves learning multiple discrimination problems in series and Concurrent Discrimination Learning (CDL) involves learning multiple discrimination problems in parallel, but LS and CDL (a) share the feature of multiple discrimination problem learning, (b) both are amenable to rote learning as opposed to conceptual learning, (c) both may embody “learning to learn” which may facilitate subsequent learning including concept learning, but (d) neither meets the definition or requirements for concept learning. Table 1 shows a revision of the LICH, compared to, for example, [4], that renames level 5, *Multiple Discrimination Learning*, and that includes CDL and LS as independent types of learning at level 5.

*Class Concept Learning* is introduced at level 6. Concept learning is defined as the ability to respond correctly to *new exemplars* of a class of discriminanda to which the animal has learned to respond. The emphasis on new exemplars means that evidence that an animal has learned a class concept requires that it respond correctly the *first time* any new exemplar of that concept is presented. The discriminanda must not be amenable to *stimulus generalization* based on physical similarities. For example and assuming the animal had human-like (trichromatic) color vision, to test for the concept of “flower” one should not use only red or near-red flowers, nor only flowers with similarly shaped petals, nor only flowers of similar sizes, as the animal might merely generalize (fail to discriminate) to a specific color, shape, and/or size, etc.

*Absolute class concepts* are those where each exemplar of the concept possesses the features that enable one to affirm that it is an exemplar without a need to compare the exemplar with other discriminanda. For example, that which distinguishes a flower from an animal is inherent in the properties of the flower. Occasionally, there may be “fuzzy” boundaries (e.g., flowers that mimic animals or animal parts and vice versa; see literature on plant-animal mimicry), but usually exemplars of flowers are easily distinguishable from exemplars of animals. *Relative class concepts* involve



discriminanda that are not inherently recognizable as a member of a class but that derive class membership from relationships with other discriminanda. The relative class concept of “oddity”, for example, is manifested in a triangle when a triangle appears with two or more circles, but a circle will manifest “oddity” when it is presented with two or more triangles. Oddity appears to have been the most studied relative class concept among nonhuman animals, and oddity (or the closely related “sameness-difference” concept) is a component of many tests of human cognitive functioning. There are further important considerations when using oddity tasks, but the reader must pursue those factors elsewhere [14,15,21,22].

*Relational Concepts I* (level 7) and *Relational Concepts II* (level 8), by definition, involve using class concepts in conjunctive, disjunctive, and conditional relationships (level 7) or in biconditional relationships (level 8). Tasks must incorporate these logical relationships as they are defined via truth-tables (see any elementary textbook of formal logic). There are many examples of nonhuman animals using class concepts in conjunctive relationships and, possibly, conditional relationships, although distinguishing between the two is deemed presently not to be feasible [4]. To revisit Thomas’s proposal that any and all learning by any and all animals (including humans) can be reduced to these eight types of learning ability, it is noted that some higher order concept learning by humans (and possibly other animals) may involve complex combinations of levels 6–8 [see 3, Tables III and IV].

Space limitations do not permit us to present methods in detail of how concept learning may be studied in nonhuman animals. However, such methodological details may be found in many of the references already cited or to be cited here; see especially the examples described in Thomas [4] and the references that he cited.

With this background pertaining to the LICH and with this special consideration of learning set formation, we may now proceed to suggest how such learning models may be used in human applications and how animal models may be used to address the kinds of higher order cognitive processes that are more likely to be used also by humans. It is suggested that far too little of such research is being done, and it is hoped that the present article will persuade others that improvements are both needed and feasible.

### 3. Application of the LICH to basic research in age-related neuropathologies

The population of aged individuals is growing due to recent medical advances. With growth in the elderly population there is a rising concern for the number of individuals who will suffer from some form of dementia as well as a concern for the substantial cost to our health care system [23]. Dementia impairs an individual’s ability to function independently due to a decrease in intellectual ability [24]. The LICH indicates eight fundamental abilities that phar-

macologists and neuroscientists might use to understand and potentially treat dementia.

Both animal lesion models as well as genetic animal models have been developed to gain understanding of the cognitive decline seen in AD. However, many of the behavioral measures used to investigate cognitive performance in these animals utilize only the bottom four levels of the LICH. We examined the abstracts for the 2005 meeting of the Society for Neuroscience (SfN) to determine the types of animal behavioral measures that neuroscientists are currently using to understand and/or treat the cognitive aspects of AD. Using keyword search terms of “Alzheimer’s disease”, “Amyloid and behavior”, and “Amyloid precursor protein and behavior”, we constructed a list of behavioral measures used with animals in relation to AD (see Table 2). Table 2 demonstrates the types of behavioral tasks reported in the 2005 SfN abstracts, their frequency of use, as well as where these tasks likely fit within the LICH.

Examination of Table 2 indicates that the majority (80%) of behavioral tasks used with animals to understand aspects of AD fit into levels 2–4 of the LICH. There were a large number (17.5%) of abstracts which contained references to a cognitive task; however, we were unable to determine the specific task used by these researchers from the abstract alone. Additionally, it is possible that we missed some abstracts and therefore some behavioral measurements with the search parameters that we used. Therefore, the percentage of tasks at different levels of the LICH might be slightly different from that reported here. However, it is clear that the overwhelming majority of behavioral tasks used fit into the lower half (levels 1–4) of the LICH.

It is important to note that placement of several of these behavioral tasks in the LICH depends only on the fundamental learning ability necessary to successfully complete the task [4]; that is, while attention, perception, memory, and species differences are important aspects to consider neurologically and behaviorally, they are not specifically addressed in the LICH [4]. Additionally, the discrimination tasks listed in Table 2, as best we could determine, used

Table 2

Reported animal behavioral tasks used to investigate aspects of Alzheimer’s disease pathology and treatment at the 2005 Society for Neuroscience Meeting, Washington, DC ( $n = 114$ )

Behavioral task	Percentage (%)	Level of LICH
Pavlovian conditioning	17.5	Level 2
Avoidance learning	2.6	Levels 2 and 3
Discrimination		
Simultaneous/successive	2.6	Level 3
Maze learning		
Barnes maze	1.75	Level 4
Hebb-Williams	0.88	Level 4
Radial maze	8.8	Level 4
T-maze	5.3	Level 4
Water maze	33.3	Level 4
Y-maze	7.9	Level 4
Operant DNMTS	0.88	Level 4
Set shifting	0.88	Level 5
Unclear cognitive task	17.5	

Table 3  
Reported animal behavioral tasks at the 2005 Society for Neuroscience Meeting Washington, DC ( $n = 441$ )

Behavioral task	Percentage (%)	Level of LICH
Habituation	2.5	Level 1
Sensitization	6.3	Level 1
Pavlovian conditioning	20.9	Level 2
Avoidance learning	2.5	Levels 2 and 3
Operant/instrumental Discrimination	5.0	Level 3
Simultaneous/successive	6.6	Level 3
Concurrent	1.6	Level 5
Operant DNMTS	2.7	Level 4
Maze learning		
Barnes maze	0.7	Level 4
Cincinnati maze	0.2	Level 4
Field expansion	0.2	Level 4
Hebb-Williams	0.2	Level 4
Radial maze	10	Level 4
T-maze	3.2	Level 4
Water maze	23.6	Level 4
Y-maze	2.9	Level 4
Set shifting	3.2	Level 5
Learning set	0.5	Level 5
Transverse patterning	0.2	Level 5
Category discrimination	0.5	Level 6
Conjunctive learning	0.2	Level 7
Unclear cognitive task	6.3	

stimuli that did not require *concept learning* ability to complete the task. Use of tasks that required concept learning would show use of level 6 of the LICH [4].

We also searched the 2005 SfN abstracts to determine more generally what animal behavioral tasks neuroscientists typically used. For the more general search, our keywords included “learning”, “cognition”, “discrimination”, “maze”, “memory”, and “conditioning”. Table 3 indicates the types of behavioral measures that were used, their frequency of use, and their placement in the LICH. Again, the overwhelming majority (87.5%) of the tasks reported in 2005 were from levels 1–4 of the LICH. Six percent of the tasks ( $n = 27$ ) were from levels 5 or possibly higher. It is possible that three of the tasks in this 6% were at level 6 or 7, but we were unable to determine that from the information in the abstracts. Fundamental to a task’s being at level 6 or 7 is that the evidence be based on first-trials with new discriminanda or on using trial-unique discriminanda. Finally, for 6.3% of the abstracts we were unable to determine what behavioral measures were used. Despite eight different fundamental learning abilities available for investigation, the strong majority of researchers were using tasks at levels 1–4 of the LICH. It is possible that we did not find all abstracts investigating animal learning, memory, or cognition with the search terms used and that other keywords might have produced a different outcome. However, Thomas [25] previously surveyed the 1997 SfN abstracts to determine the types of behavioral measures used to investigate pharmacological correlates of “higher order” cognitive processes. Thomas reported a similar pattern of behavioral tasks used by neuroscientists at the 1997 SfN annual

meeting and that 100% of the tasks used were between levels 1–4 of the LICH hierarchy. Therefore, other search terms used here might have created slight changes in the percentage of use for each level of the hierarchy, however, we believe that the vast majority of tasks will still involve only the lower four types of learning (see Table 1).

We are not suggesting that researchers can not gain substantial insight into neurological disease and cognitive decline when using only behavioral tasks requiring level 1–4 learning abilities. Most advances in medicine, neuroscience, and pharmacology have been made using such behavioral measures. However, we are suggesting that much more might be gained by using animal models that involve the kinds of cognitive abilities that are more likely used by humans. If experimental animals, particularly rats and mice, are to provide the best possible models for investigating the kinds of cognitive abilities that might be affected by comparable brain damage or disease in humans, it will be important to expand the range of cognitive abilities being tested. Animals are indeed capable of solving tasks which require use of levels 5–7 of the LICH, although there is no current experimental evidence for biconditional reasoning (level 8) in non-human animals (Thomas, 1996).

#### 4. Functional neuroanatomical considerations

As has been argued by Kolb and Wishaw [26, p. 109] “There is no strong evidence for unique brain-behavior relations in any species within the class Mammalia, including *Homo sapiens*”. This statement is not meant to imply that inter-species differences are non-existent or of trivial importance, but to emphasize that homologous brain structures perform analogous functions across species. Thus, the neuroanatomical structures involved in specific cognitive processes in humans have their counterparts in other mammalian species. This is true for the posterior neocortical structures that are involved in various sensory and perceptual functions, for the anterior neocortical tissues involved in motor functions, and association cortices intercalated between and/or surrounding these areas [26, pp. 105–108].

Indices of the evolution of the brain (e.g., encephalization quotients) [27] in mammals have been associated with an increase in the number of cytoarchitecturally and functionally distinct neocortical modules capable of increasingly refined processing. For example, the visual cortex of the rat may be differentiated into three or perhaps four major functionally distinct regions [28–30], while the auditory cortex can be differentiated into two or three such regions [31]. Homologous structures in the brain of Rhesus macaque include at least twice as many functionally distinct regions.

Efferents from the posterior parietal and temporal cortices feed forward to innervate the rat homologue of the primate prefrontal cortex [32] just as they do in the primate brain [33,34]. It must be acknowledged however that whether or not the medial dorsal frontal cortex in rat is a true homologue of primate prefrontal cortex remains in

question. Preuss [35] has made a convincing argument on the basis of cytoarchitectonic evidence that the medial “prefrontal” cortex in rat shares more in common with the primate premotor, and anterior cingulate, and orbitofrontal cortex of primates than it does the dorsolateral prefrontal cortex.

The rationale for the foregoing discussion of functional neuroanatomical relationships between rodents, nonhuman primates, and humans is that tissues within the inferior temporal, posterior parietal, and prefrontal cortices in both human and nonhuman primates that have been most frequently associated with higher cognitive functions [26,36,37], and damage within these regions results in cognitive impairments without significant sensory or motor impairments. Thus, many questions concerning the underlying neuroanatomical bases of higher cognitive functions in humans that are affected by cerebral trauma, exposure to toxins, progressive neuropathologies, and potential pharmacological and behavioral treatments for these conditions might be addressed in nonhuman species, and in some cases, with rodents.

*Investigations of “Higher Cognitive Functions”.* Regarding creativity, the topic of this Special Issue, the frontal lobes have most often been identified as especially involved in “higher cognitive” and “executive” functions. As Kolb and Whishaw [26; p. 466] lamented, “Historically, claims about the function of the frontal lobes have been extravagant and extreme. From the time of Gall until the 1930’s, the frontal lobes were thought by most to be the seat of the highest intellect. Functions as varied as ‘abstract behavior’, foresight, intelligent synthesis, ethical behavior, affect, and self-awareness were proposed by a variety of writers”.

Anatomically the frontal lobes of humans [37] and rhesus monkeys (*Macaca mulatta*) have been divided into as many as 13–15 distinct regions based on cytoarchitectonic criteria. Functionally, however, the frontal lobes are typically divided into motor areas (supplementary motor, premotor, and primary motor, and frontal eye fields), and prefrontal cortices. Rose and Woolsey [38] noted that much of the non-motor frontal cortex receives projections from the mediodorsal nucleus of the thalamus. Definition of a similar territory, on the basis of thalamic afferents, along the mid-sagittal portion of the anterior frontal neocortical tissue of rodents has also been identified [39].

Functionally the prefrontal cortex in primates is often divided into two main sectors, the dorsolateral prefrontal cortex and the orbitofrontal cortex, although there is considerable evidence for additional functional division. As the nomenclature suggests, the dorsolateral areas are dorsal and lateral in the frontal lobe, while orbitofrontal cortex lies at the base of the calvarium above the ocular orbits. There are other areas such as inferior frontal cortex, areas 11 and 12, and medial frontal cortex, areas 25 and 32 [26, p. 464] located within the region described as prefrontal. It has long been known that lesions in frontal regions, via trauma, invasive tumorous growths, or progressive neuropathology of the frontotemporal type (e.g., Pick’s Dementia), can lead to

severe deficits in working memory and higher cognitive abilities, often labeled “executive functions”. Significant changes in personality and in socially inappropriate behavior also have been reported consistently.

As discussed earlier there has been a dearth of information concerning the neuroanatomical, neurochemical, and neuropathological sequelae associated with both normal and impaired conceptual functions. Only limited progress has been made in the development of neuropharmacological and behavioral strategies for mitigating these important health and societal problems, and we suggest that progress has been diminished by the underutilization of appropriate animal methodologies to address conceptual abilities and other higher cognitive functions. However, a literature exists to show that addressing higher cognitive functions in animals is more feasible than what has been achieved in the neurobehavioral literature to date.

*Learning set formation tasks and application to frontal lobe function.* In humans, damage to the frontal cortex has been associated with impaired social inhibition, impaired egocentric but not allocentric visuospatial orientation, impaired response inhibition, poor temporal memory, deficits in behavioral inflexibility, and impairments in the discovery of strategic solutions to novel problem solving situations [26,37]. While lesions anywhere within the prefrontal cortex of either hemisphere can lead to difficulties in these cognitive functions, it is the orbitofrontal tissues [40–42], and particularly Brodmann’s area 8 located in the dorsolateral prefrontal cortex of the left hemisphere [43,44] that has been most associated with perseveration (i.e., repetition) of previously learned response preferences.

One task considered especially sensitive to prefrontal processes in humans is the Wisconsin Card-Sorting Test. Here the examinee is presented with four stimulus cards that differ in color, geometric form, and number of forms on the card. The task is to sort the cards into piles on the sole basis of being told whether each response was correct or was incorrect. The examinee must discover the appropriate sorting strategy. When a predetermined criterion for learning a strategy has been met, the sorting strategy changes without warning. Beginning with the strategy of sorting by color, the strategy changes to sorting by form, and then to sorting by the number of elements on the card (one, two, three, or four). The sequence of shifting strategies continues until all 126 cards have been sorted. The ability to shift response strategies is impaired in people with frontal lobe injuries. They tend to perseverate with a learned sorting strategy despite the change in feedback intended to guide them to change strategies, and as observed by one of us (WFM), they sometimes report that they know that what they are doing is incorrect but they cannot inhibit it. It is useful to note that recent neuropsychological studies with schizophrenic patients indicate that similar problems with response inhibition are partially mitigated by administration of atypical antipsychotic medication [45].

The acquisition of the win-stay lose-shift strategy in the learning set task has some similarity to the Wisconsin

Card-Sorting Test. Being able to shift behavioral strategies would be a prerequisite psychological process to creativity. It is noteworthy that Rhesus monkeys with injuries to the prefrontal cortex perform poorly in object discrimination learning sets [46,47], and animals with orbitofrontal lesions perform significantly more poorly than animals with more laterally placed lesions [48]. Also a recent neuroimaging study used positron emission tomography to examine regional cerebral blood flow while Rhesus monkeys learned what was described as a “simple vasomotor task”, multiple visual discrimination tasks (VDM), and what the authors believe to be learning set formation whereby the monkeys percentage correct responses on trials with novel stimuli exceeded 90% [49]. There are considerable differences between the methodology used in this study and that originally described by Harlow [16,17] and, unfortunately, the authors did not discuss performance on trial 2 of the trials thought to reflect learning set formation. Also there appear to be differences between the methodologies to present discriminanda in the concurrent object discrimination tasks traditionally employed and the computer generated stimuli used in the VDM tasks. Nevertheless, this study reports that activity in the orbitofrontal cortex and putamen is high in pre-learning set visual discrimination learning. Once the animals show behavioral efficiency by acquiring novel discriminations rapidly with few errors, activity in the former two structures diminishes while it clearly increases in the lateral prefrontal cortex and anterior inferior temporal cortex. These results are interpreted as showing that the “lateral prefrontal cortex may mediate the higher-order representational process for selections as well as suppress the functional network between striatum and anterior inferotemporal cortex that regulates the non-cognitive, habit learning with short latency of response in the VDT” [49]. The metabolic activity results correspond well with expectations that would be based on lesion research.

*Comparable tasks used with human and nonhuman animals.* One version of a learning set task is reversal learning. Here the subject, human or non-human, learns to associate a particular stimulus (stimuli may be visual, olfactory, kinesthetic, etc.) with reward. Reward can consist of either appetitive incentives such as access to food or water [50] or escape from aversive conditions as in finding the submerged platform in a water T maze [51]. When criterion to demonstrate learning is reached, the previously nonrewarded stimulus is now associated with reward. A series of reversals is continued. Zhou and McDaniel [51] used a water T-maze spatial reversal task to study learning in rats prepared with bilateral medial prefrontal lesions and normal controls. Both groups learned the initial discrimination (viz., turn right to find the escape platform) rapidly and at equivalent rates. Normal rats soon learned to make a reversal after making only one or two errors, but rats with medial prefrontal lesions perseverated on the previously correct spatial choice and required considerably more trials to learn each

new reversal. This behavioral methodology could be applied to many pharmacological agents that might have neuroprotective or nootropic properties.

A comparable task was developed to screen qualitatively the learning abilities of individuals with severe cognitive dysfunctions [52] such as mental retardation and advanced dementia. The examinee is first allowed to observe while a reinforcer (piece of candy, coin, etc.) is placed under one of two cups differing in diameter, color, and texture. The spatial positions of the cups are shifted several times and the examinee encouraged to retrieve his/her reward. When this has been learned, observing placement of the reinforcer under a cup is prevented but the same cup associated with reward in observation learning trials continues to cover the reinforcer. The left–right spatial positions of the cups is randomized across trials. If the object discrimination task is learned testing now continues with reversed reinforcement contingencies. That is, the previous nonrewarded cup now hides the reinforcer. This may continue for many reversals. This task involves learning processes as low as level 3 (Stimulus–Response Learning) and as high as level 5 (Learning Set Formation). The testing procedures readily distinguished between individuals diagnosed with Moderate Mental Retardation from those diagnosed with Severe Mental Retardation. The utility of this approach is that the results allow professionals involved in providing services to comment on rates of general acquisition, the client’s ability to profit from positive and negative feedback, the client’s level of behavioral flexibility when conditions change, and problems of response inhibition. Being able to comment on an individual’s flexibility as reflected on the object reversal task can be useful in designing individualized educational and habilitation programs that are sensitive to an individual’s cognitive capacity. Potentially, an easily administered task such as this might also be used to examine the cognitive enhancing properties of drugs intended to slow the progression of a dementia through neuroprotection (e.g., memantine) or enhancement of diminished neurotransmitters (e.g., donepezil).

## 5. Conclusions

The ability to use a learning set is an example of behavioral flexibility which is commonly listed as one aspect of executive functioning. Executive processes are known to decline in dementia and are often characterized as the ability to evaluate, organize, and reach new goals, as well as the ability to adapt (showing flexibility) when confronted with novel problems [53]. The ability to use a learning set requires flexibility in order to maximize reward and provides a good behavioral measure for the study of human executive functioning and for cognitive decline.

There is extensive research demonstrating the ability for several different species to acquire learning sets (level 5 of the LICH). Evidence for learning set has been seen in birds [54–56], cats [57,58], dolphins [59], ferrets [57] mink [57], skunks [57], and nonhuman primates [16,18,60–63].



Additionally, when olfactory discriminanda are used, rats can quickly demonstrate use of learning set [14,15,64–67].

Changes in the frontal cortex and medial temporal cortex have been linked to problems with executive functioning [68]. As we indicated earlier, animal lesion models with monkeys have found that extensive damage to the prefrontal cortex [46–48] and lesions to temporal neocortex [69,70] impair learning set formation. With rats one can investigate both the acquisition of a learning set [15,65] as well as the retention of a previously learned learning set [71]. Using rodents, researchers have found that lesions to the medio-dorsal thalamic nucleus [72], the fimbria-fornix [73], and lesions to the nucleus basalis magnocellularis [71] significantly disrupt learning set performance. Therefore, there is research on the neuroanatomical structures and neurochemical systems associated with use of learning sets in rodents. However, learning set formation in rats apparently has not been used for research on therapeutic interventions associated with cognitive decline due to dementia such as Alzheimer's disease and neither for the investigation of potential neuroprotective agents. Learning set formation as a tool for behavioral pharmacologists and neuroscientists remains a relatively unused resource. With respect to creativity, we would argue that the demonstration of behavior flexibility in the learning set task, even as simple as reversal learning, must be a prerequisite for creative solutions to novel problems. Thus, finding areas of the brain that are essential for behavioral flexibility implicate areas in more advanced species that might be responsible for creativity.

Use of learning set, especially in a reversal learning task, is an easy way to increase the cognitive demands of tasks used in the neurosciences. Thomas [4] mentioned the possibility of adding concept learning requirements to discrimination tasks as a way to increase cognitive demand. Our examination of the 2005 SfN abstracts indicated that scientists are using discrimination learning tasks in their research (see Tables 2 and 3) but they are tasks that do not involve or require concept learning. For example, instead of using a simple discrimination learning problem, such as discriminating a triangle from a circle or square, one might try using many different exemplars of triangles (enough to have unique triangles on each trial or enough to use only the data from the first trials of repeated problems beginning with new triangles) and equally many different exemplars of an easily discriminated geometrical form, such as heptagons. Successful performance on such a task would involve more than merely memorizing the features of a particular triangle and would require learning and using the concepts of triangularity and heptagonality. This is only one of many examples of tasks that require concept learning that rats seem likely to be able to learn and perform successfully.

There is a rich literature, only partially referenced here, with intact, normal nonhuman primates, birds, cats, dolphins, ferrets, mink, skunk, and rats showing that they are capable of higher level cognitive functions than the abilities typically studied by neuroscientists interested in understanding animal parallels of normal and aberrant cognitive

functions. We suggest that the learning and cognitive abilities presented in the LICH here are foundational for creative thought. The neuroanatomical substrates of such processes might be advanced by applying methods such as those of Yokoyama et al. [49] in conjunction with lesion and genetic animal model experiments that use tasks that demand the higher level, strategic learning abilities and conceptual abilities discussed here.

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