International Journal of Comparative Psychology, 2011, 24, 36-59.

Individual Differences in Animal Intelligence: Learning, Reasoning, Selective Attention and Inter-Species Conservation of a Cognitive Trait

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Humans' performance on most cognitive tasks are commonly regulated by an underlying latent variable (i.e., "general" intelligence), and the expression of this latent modulator of cognitive performance varies across individuals. While "intelligence" in humans is easily recognized, a precise definition of this trait has proven elusive, and has impeded efforts to compare the emergence of this trait across species. Here we describe our efforts to characterize this cognitive trait in genetically heterogeneous laboratory mice. Using batteries of as many as eight learning tasks and various principal component analysis regimens, we have found a robust general factor that accounts for nearly 40% of the variance of individual animals across all tasks. This "general learning factor" is not attributable to variations in stress reactivity or exploratory tendencies. However, like human intelligence, this general factor covaries with the efficacy of selective attention and working memory capacity. Importantly, we also find that general learning abilities covary with animals' performance on novel tests of reasoning. In total, this work indicates that learning abilities, attentional control, and the capacity for reasoning, features that constitute both colloquial and formal definitions of human intelligence, are commonly regulated in individual genetically heterogeneous mice. These results suggest an evolutionary conservation of the qualitative and quantitative properties of intelligence, and indicate that like humans, sub-human animals express individual differences in this trait.

For much of the history of animal studies of learning and memory, research has focused primarily on the processes and mechanisms that regulate single domains of learning (e.g., spatial abilities or Pavlovian conditioning). While this tactic has been successful in delineating the neuroanatomical substrates of certain forms of learning and even learning domains (e.g., Berger, Laham, & Thompson, 1980; Eichenbaum & Lipton, 2008; Fanselow & LeDoux, 1999; Holland & Gallagher, 2006; Ledoux, 2007), it has left unexplored those aspects of learning that are common across all domains. Conversely, studies of humans have focused more extensively on the mechanisms that underlie *general* influences that impinge on all cognitive abilities (i.e., general intelligence). However, such studies are constrained by certain practical and ethical considerations that do not similarly limit studies of laboratory animals. Therefore, a synthesis of these two approaches would be of great virtue in beginning to elucidate the structure of and mechanisms underlying general intelligence.

Here we will describe our efforts to isolate a general influence on cognitive performance in genetically diverse mice, and will explore the extent to which that trait is qualitatively and quantitatively analogous to the concept of "intelligence" as it is applied to descriptions of human cognitive performance.

This work was supported by grants from the National Institute of Aging (R01AG029289 and AG022698) and the Busch Foundation. Thanks are extended to Alexander Denman-Brice, Kenneth Light, and Danielle Colas for many discussions that helped refine this work. Correspondence concerning this article should be addressed to Louis D. Matzel, Department of Psychology, Rutgers University, Piscataway, NJ, 08854, U.S.A. (matzel@rci.rutgers.edu).

What is “Intelligence”?

Before we can begin to assess the possibility that mice express a trait that is analogous to intelligence, it is necessary to at least attempt to constrain or define our discussion of this trait so that it may be quantified. In 1995, a committee of the American Psychological Association stated that:

> *Individuals differ from one another in their ability to understand complex ideas, to adapt effectively to the environment, to learn from experience, to engage in various forms of reasoning, to overcome obstacles by taking thought. Concepts of ‘intelligence’ are attempts to clarify and organize this complex set of phenomena.*

In an article in the Wall Street Journal (December 13, 1994) signed by 52 intelligence researchers, it was asserted that intelligence was “a very general mental capability that, among other things, involves the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly and learn from experience. It reflects a broader and deeper capability for comprehending our surroundings.”

The above definitions, although provided by renowned experts on intelligence, are decidedly nebulous in their content, and at the same time, expansive in their scope. Nevertheless, despite the ongoing “expert” debate as to what constitutes “intelligence,” these definitions would differ little (if only in form) from colloquial description of the trait that one might hear from a random sample of college undergraduates. Thus more than 100 years after Spearman (1904) first described the concept of “general intelligence” (i.e., *g*), we still grapple with its definition, but much like pornography, tend to know it when we see it. In this regard, quantification of intelligence might best be relegated to performance on psychometric tests. The rationale for psychometric tests are roughly based on Spearmen’s early observation that performance on a wide range of cognitive tasks are positively correlated, and as such, can be reduced to a single index of aggregate performance across the battery of tests. While controversy persists regarding exactly what is measured by psychometric tests of intelligence (e.g., the Stanford-Binet, Wechsler Adult Intelligence Scale, the Raven’s Progressive Matrix), this controversy arises in large part from the lack of consensus and/or vague definitions of intelligence itself. What is certain is that these tests are strongly predictive of important social outcomes, including educational and career success (Gottfredson, 1998; Jensen, 1998). To quote Gottfredson (1998):

> *no matter their form or content, tests of mental skills invariably point to the existence of a global factor that permeates all aspects of cognition. This factor seems to have considerable influence on a person’s practical quality of life. Intelligence as measured by IQ tests is the single most effective*

> *predictor known of individual performance at school and on the job as well as many other aspects of "well being."*(p. 24)

In conclusion, contemporary "definitions" of intelligence tend to be vague, broad, and to some degree, a matter of debate (Sternberg, 1985). Nevertheless, psychometric tests of intelligence do appear to characterize a trait captured in both colloquial and empirical definitions of intelligence, i.e., the ability to understand, learn, and reason. Thus to explore a trait analogous to intelligence in laboratory animals, we should devise tests that characterize this same set of skills. To this end, we have begun to characterize the performance of mice on batteries of tests that represent diverse learning skills, reasoning abilities, and the capacity for selective attention (a process presumed to regulate these other cognitive skills).

General Learning Abilities in Genetically Heterogeneous Mice

In our earliest work in this area, we explicitly avoided any reference to or consideration of intelligence *per se*, and instead, focused our efforts on the quantification of a general influence on the ability of laboratory mice to acquire efficient responses across a diverse set of learning tasks. To this end, genetically diverse (outbred) CD-1 mice were tested in a battery of five common learning tasks, each of which made unique sensory, motor, and information processing demands on the animals (Matzel et al., 2003). In this regard, this test battery was analogous to the design of "classic" human intelligence tests, wherein various components of the battery are presumed to impinge on different information processing skills (i.e., "domains" of information processing). The tasks in this battery were rudimentary in nature (associative fear conditioning, passive avoidance, path integration, odor discrimination, and spatial navigation) such that all animals could eventually acquire the target responses with equal efficiency, but did so at different rates. Animals that performed well (i.e., exhibited relatively rapid acquisition) in one task tended to perform well in other tasks in the battery. This relationship was captured by a correlational analysis of animals' performance on all learning tasks. A positive correlation of individuals' rate of acquisition across all tasks was observed, and principal component analysis indicated that 38% of the variance across tasks was attributable to a single factor, which we described as "general learning ability." However, in published commentaries on this article, the characterization of these mice was described as reflecting a trait that was qualitative and quantitatively analogous to the trait that is described in humans as "intelligence" (Blinkhorn, 2003). Since the time of this report (based on an analysis of 56 animals), similar results have been obtained in mice tested on as many as nine cognitive tasks (Matzel, Grossman, Light, Townsend, & Kolata, 2008), and in a comprehensive test of 241 mice, Kolata, Light, and Matzel (2008) reported a hierarchical structure of the general cognitive abilities of mice (where a general factor influenced domain-specific factors, including spatial abilities). This hierarchy of control is similar to that thought to underlie human intelligence test performance. Figure 1 provides an illustration of the summary data of performance of a poor, average, and good learners drawn from a sample of 241 mice tested on five learning tasks, as well as the distribution of general learning performances of all of the animals in this data set. As is evident from this figure, a roughly normal distribution of the aggregate performances of individual mice across this battery of tests was observed, and such normalcy is a defining characteristic of humans' performance on standardized intelligence tests.

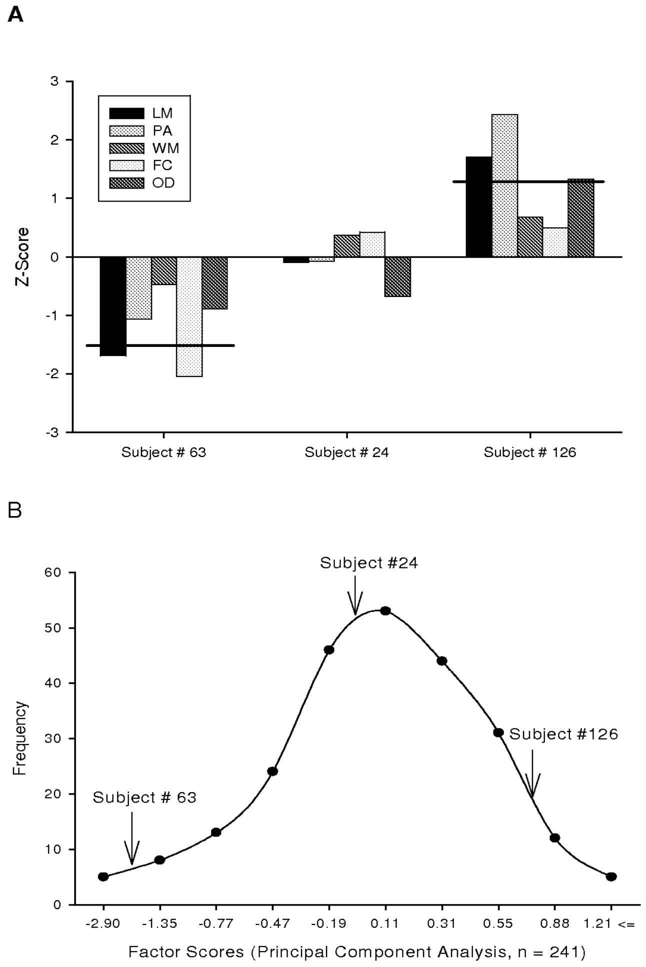


Figure 1. A) Sample data from three animals that were run through the learning battery (LM = Lashley maze, PA = passive avoidance, WM = spatial water maze, OD = odor discrimination, FC = fear conditioning). Values indicate the z-scores of the individual animal's learning rate. Performances across the different tasks are highly related such that one could designate a good learner (subject # 63), an average learner (subject # 24) and a poor learner (subject #126). The solid lines indicate the average score across trials. B) Normal distribution of factor scores extracted from a principal component factor analysis performed on the learning data from 241 mice tested on the five learning tasks. Arrows indicate where the three sample animals (subject # 63, subject #24, and subject # 126) fall in the distribution. (Adapted from Kolata et al., 2008)

Sensory, Motor, and Non-Cognitive Influences on General Cognitive Abilities

In our first paper on individual differences in general learning abilities (Matzel et al., 2003) , we observed a relationship that suggested the possibility that general "learning" abilities might not reflect variations in learning *per se*, but rather, an indirect effect on learning *performance* by exploratory tendencies and/or stress reactivity. In particular, a strong direct correlation was observed between animals' level of exploration and their aggregate performance on the learning battery. This suggested the possibility that elevated exploration promoted better learning. It is notable in this regard that the degree of preference for novelty in human infants is positively correlated with later performance on standardized IQ test batteries (Bornstein & Sigman, 1986; Vietze & Coates, 1986). Furthermore, since exploration was presumed to be influenced by stress reactivity, it was possible that differential stress responses could account for variations in nominal "learning" abilities, since stress can itself impair (or in some case enhance) an animal's performance on tests of learning (Shors, 1998). Although untested, it was also possible that variations in aggregate learning performance did not reflect differences in learning ability *per se*, but instead, differences in some aspect of sensory or motor fitness.

The above possibilities were assessed in a series of experiments. First, we determined the relationship between 31 measures of sensory/ motor abilities, fitness, fear/stress sensitivity, and the general learning abilities of individual animals (Matzel et al., 2006). In no instance were we able to detect a relationship between measures of simple fitness or sensory/motor function and general learning performance. For instance, measures of balance, pain sensitivity or reactivity, running speed, swimming speed, and overall activity all loaded weakly and inconsistently on factors on which performance on learning tasks loaded heavily in a principal component analysis. Again however, animals' exploratory patterns in novel environments (an open field and an elevated plus maze) loaded heavily and consistently with performance on tests of learning. Specifically, the extent to which animals' engaged in exploration of areas of environments that are commonly asserted to promote stress responses were positively correlated with performance on learning tasks. Performance measures such as the percent of activity in open quadrants of the open field, percent of time and number of entries into open arms in the elevated plus maze, latency to enter the first open arm, and proclivity to enter *new* arms in the plus maze were positively correlated and all loaded heavily with learning performance on a single factor extracted by principal components analysis.

In contrast to measures of exploration, common measures of fear loaded weakly and inconsistently with measures of learning. In particular, fecal boli counts during exploration of the open field, shock-induced freezing, and startle-induced escape responding were unrelated to animals' exploratory patterns or their general learning abilities. This pattern of variable loading suggests that the relationship between exploration and learning was *not* attributable to variations in animals' expression of fear or their sensitivity to fear-evoking situations or stimuli.

This is critical, as laboratory situations (e.g., handling, novel environments, aversive stimulation) designed to assess learning in animals can reasonably be expected to promote fear. These results mitigate the possibility that variations in individuals' sensitivity to fear might underlie the variations in general learning abilities that we observe in laboratory mice.

Exploration of the open quadrants of a novel open field or the open arms of an elevated plus maze is often interpreted as an indication of an animal's proclivity for novelty seeking, and/or may reflect the degree to which an animal experiences stress in the unfamiliar open environments (Anderson, 1993; Kabbaj, Devine, Savage, & Akil, 2000). While the underlying nature of this relationship between novelty seeking and learning/intelligence is unknown, it is possible that animals more engaged by novelty are more likely to recognize (or attend to) those environmental relationships upon which learning depends. Relatedly, animals that are prone to novelty seeking may be less susceptible to the experience or physiological consequences of stress, which in many instances can impede learning (Shors, 1998). This later possibility was assessed by examining the relationship between animals' serum corticosterone levels (a physiological index of stress) and their propensity for exploration. Of particular interest was the nature of this relationship under basal conditions relative to the relationship under conditions in which animals were experiencing a level of stress comparable to that which might accompany exploration of a novel environment. Of note, no relationship was found between basal corticosterone levels and individual animals' propensity to explore the open quadrants of the open field or the open arms of an elevated plus maze. Similarly, the elevated corticosterone levels associated with a mild stressor (confinement on an elevated platform) were unrelated to animal's level of activity in the open quadrants of an open field. A tendency toward a relationship between stress-related corticosterone levels and time spent in the open arms of the elevated plus maze was observed, but in this case, the correlation was such that *higher* serum corticosterone was associated with a proclivity to spend *more* time in the open arms (Matzel et al., 2006). The direct relationship between physiological stress reactivity and the propensity for exploration suggests that it is unlikely that *reduced* sensitivity to stress could underlie an enhancement of general learning abilities.

Upon initial consideration, it is somewhat surprising that fear and/or stress sensitivity are not inversely related to animals' exploratory tendencies in novel environments, particular when those tendencies are such that the exploratory pattern exposes animals to environments that are known to evoke stress responses (for results similar to those reported here, see (Dellu, Piazza, Mayo, Le Moal, & Simon, 1996; Piazza et al., 2005). However, using a similar factor analytic approach with different dependent measures of stress, a similar lack of covariance between these variables has been previously observed. For instance, Overmier, Murison and Johnsen (2003) have reported that the initial propensity of rats to explore a novel environment was unrelated to the likelihood or extent of stress-induced ulceration. Similarly, Overmier et al. (2003) found no relationship between common measures of fear and animals' propensity for exploration or their sensitivity to stress-induced ulceration. It is notable that in the present studies, fecal boli counts in a novel open field *were* positively correlated with the level of serum corticosterone associated with mild stress. Given the absence of a relationship between these fecal boli counts and both exploratory patterns or learning abilities, this result further suggests that fear and/or stress sensitivity cannot account for variations in general learning abilities.

In total, these results provide further evidence for the existence of an influence on animals' learning abilities that transcends limited learning domains, and that is independent of the sensory, motor, motivational, and information processing demands of specific learning tasks (also see Galsworthy, Paya-Cano, Monleón, & Plomin, 2002; Locurto, Benoit, Crowley, & Miele, 2006; Locurto, Fortin, & Sullivan, 2003). Furthermore, variations in individuals' general learning abilities do not appear to be attributable to individual differences in fear responses or the sensitivity to (or physiological consequences of) stress. Nevertheless, we repeatedly observed a strong and consistent relationship between animals' tendency to explore stress-inducing novel environments and their general learning abilities. Of course it is possible that these two classes of behavior (learning and exploration/novelty seeking) are regulated in common but do not otherwise influence each other. A more intriguing possibility is that animals' propensity for exploration predisposes them to encounter those contingencies upon which learning depends, and thus is a determinant of general learning abilities.

This later possibility was assessed in two ways. First, Grossman, Hale, Light, Kolata, and Matzel (2007) treated animals with a dose of an anxiolytic (chlordiazopoxide) that promoted an increase in exploratory behaviors but which had no measureable effect on sensory/motor behaviors or pain sensitivity. Despite the increase in exploration, no benefit of the anxiolytic could be observed on individual learning tasks or on aggregate performance in the battery of learning tests. In fact, nonsignificant tendencies were observed for the anxiolytic treatment to *impair* learning, an effect that has been observed elsewhere (Kroon & Carobrez, 2009; Scaife et al., 2007). Light et al. (2008) provided a more direct test of the possibility that increases in exploration might promote a commensurate facilitation of general learning abilities. To this end, Light et al. exposed animals to a series of novel and varyingly complex environments over a sequence of 12 days. This "adaptation to novelty" promoted a profound and long-lasting (at least 30 days) increase in the propensity for exploration when the treated animals were again tested in yet another novel, but unique, environment (an elevated plus maze). Despite this increase in exploratory behavior, these animals exhibited no overall improvement in performance in our battery of learning tasks. In total, these results suggest that while general learning abilities and exploratory behaviors consistently co-vary, the degree of exploration has no direct causal impact on animals' aggregate performance on batteries of diverse learning tasks. What then is the basis for this relationship between cognitive performance and exploration? Data from our laboratory suggests that far from being a "non-cognitive" measure, an animal's propensity for exploration is in fact modulated by its capacity for learning. According to this reasoning, exploration of the more stress-inducing areas of a novel environment (e.g., the open arms of an elevated plus maze) begins to emerge at the time at which animals adapt to the less stress-inducing aspects of that environment (e.g., the closed arms of an elevated plus maze). Consequently, faster learners adapt more quickly, and thus move to explore new areas sooner. Our recent, more detailed analysis of the behavior of mice in the open field and elevated plus maze, as well as other exploratory behaviors, has confirmed this possibility (Light et al., manuscript under review; for related results, see Poucet, Chapuis, Durup, & Thinus-Blanc, 1986).

The Relationship of Working Memory to General Cognitive Abilities in Mice

"Higher cognitive functions" (such as reasoning, comprehension, and learning) are the hallmark of contemporary intelligence test batteries, and form common colloquial descriptions of "intelligence." Thus it is not surprising that "working memory" (or at least some of its sub-components) has come to be viewed by some as the potential latent factor which underlies general (fluid) cognitive abilities, i.e., intelligence (e.g., Engle, Tuholski, Laughlin, & Conway, 1999; Mackintosh, 1998; Matzel & Kolata, 2010). Accordingly, variations in (components of) working memory efficacy have been proposed to regulate individual differences in intelligence.

Although measures of list retention abilities have appeared in intelligence test batteries since their earliest descriptions (see Dempster, 1981), Daneman and Carpenter (1980) reported that simple span (i.e., "memory span" or the ability to accurately recall a list of items, in this case, words) was uncorrelated with reading comprehension (on a Scholastic Aptitude Test, a task thought to be representative of intelligence). In contrast, complex span (the ability to retain and recall the last words in a series of related sentences) was strongly correlated with reading comprehension, although the actual list of words was identical in the simple and complex span tasks. While both simple and complex span each tax storage abilities, only complex span is believed to reflect processing abilities, i.e., the capacity to retain information while simultaneously using that information to complete a directed task. Thus Daneman and Carpenter proposed that processing components of working memory were more critical to the establishment of intelligence than were simple storage abilities. Numerous behavioral studies have supported this contention (e.g., Ackerman, 2005; Colom, Rebollo, Palacios, Jaun-Espinosa, & Kyllonen, 2004; Conway & Engle, 1996; Engle et al., 1999; Sub, Oberauer, Wittman, Wilhelm, & Schulze, 2002). In converging support, brain image analyses have indicated that a wide range of higher cognitive tests (i.e., ones that simultaneously tax storage and processing abilities) engage areas of the frontal cortex (particularly the dorsolateral prefrontal cortex; see Section 4 below) which are thought to be critical for the efficient implementation of working memory (Gray, Chabris, & Braver, 2003; Haier, Jung, Yeo, Head, & Alkire, 2004), and activity in the dorsolateral prefrontal cortex during intelligence testing is predictive of overall performance on those tests (Conway, Kane, & Engle, 2003).

Based on the above considerations, and having established a conceptually and quantitatively sound method with which to assess the general learning abilities of laboratory mice, we began to assess the relationship of working memory to these abilities. It is notable that in laboratory mice, these comparisons can be made without some of the more daunting complications associated with similar work in humans (e.g., phonological processes or prior experience). To begin to assess this relationship, we tested mice on a procedure adapted from an earlier one described by Roberts and Dale (1981). In this task, animals were first tested in the learning battery described above. These animals were then trained to asymptotic levels of performance in two separate eight-choice radial arm mazes. In this task the animal could collect eight pieces of food in distinct locations radiating out from a central hub. A return to a location from which food had already been obtained was scored as an error. After stable performance had been established in both mazes, two aspects of working memory were assessed. First, after several choices in one of the mazes, animals were confined to the central hub for varying periods of time before being allowed to make further choices in that maze. Errors following confinement increased as a function of the length of confinement, a result thought to reflect the decay of information in short-term storage. However, individual differences in the degree of disruption after confinement were only weakly related to animals' general performance on the cognitive test battery. This result is comparable to that obtained with similar manipulations in humans, where it has been reported that short-term memory duration is weakly or inconsistently correlated with performance on standardized intelligence tests. In a second manipulation, mice were required to concurrently operate in each of the two mazes, i.e., several choices in one maze alternated with choices in a second maze. Since the spatial cues used to guide the animals' choice were shared across the two mazes, this manipulation was thought to tax a process more analogous to working memory capacity, i.e., information from one task had to be retained for subsequent use while performing in a second, overlapping task (by analogy, consider the Daneman and Carpenter task described above). As anticipated, these competing demands promoted an increase in errors (with a non-linear increase in errors as the number of choices increased). The number of errors committed by individual animals was inversely related to their aggregate performance on the cognitive test battery (Kolata et al., 2005). This led to the conclusion that working memory capacity, but not short-term memory duration, was related to the animals' performance on the learning test battery.

As noted above, working memory is not a singular process, but instead encompasses both the storage of information as well as the processing and integration of information (Baddeley, 2003; Jarrod & Towse, 2008). The above experiment could not discern the relative contribution of these different aspects of the working memory system to the correlation with general cognitive abilities, and so a second series of experiments (Kolata, Matzel, & Light, 2007) was designed to assess these relative contributions. First, simple span abilities were assessed by requiring mice to maintain the memory of up to six visual symbols associated with food rewards. A moderate correlation (r = 0.38) was observed between this measure of simple span (the number of items accurately remembered) and individual animals' aggregate performance in a battery of six learning tasks. A second task was employed with which we could assess the efficacy of these animals' selective attention. This task was modeled after the human Stroop test (Stroop, 1935). In a typical Stroop test, a subject is required to identify the font color of a word that is briefly (e.g., 50 ms) presented. In the simple form of this test, subjects' accuracy is normally quite good. However, if the color of the font conflicts with the meaning of the word, e.g., if a red font spells the word "BLUE" (i.e., **BLUE**), performance degrades such that the latency to respond is extended and/or response errors begin to accrue. This degradation in performance is thought to reflect a highly specific failure of selective attention. In the Stroop-like task that we adapted for mice (Fig. 2), the animals learned a three-choice visual discrimination in a context referred to as "A" (Vis-A) and a three-choice olfactory discrimination in a context referred to as "B" (Olf-B). After stable performance had been attained in both tasks, animals were occasionally tested under conditions of high interference, i.e., both odor and visual cues were simultaneously presented in Context A (Vis/Olf-A; the context which signaled the relevance of visual cues) or in Context B (Olf/Vis-B; the context which signaled the relevance of olfactory cues). Absent the interference promoted by these task-relevant distracters, animals' performance on both the visual and olfactory discriminations was nearly perfect. However, when the task-relevant distracters were added to the test context (e.g., olfactory cues were present in the visual discrimination context), errors began to accumulate. The degree to which an animal committed errors under conditions of interference was strongly correlated ($r = 0.50$) with their aggregate performance in the cognitive test battery. Although no task can be asserted to be process-pure, this animal analog of the Stroop task makes no nominal demands on either short-term memory duration or simple span abilities, and instead requires the animal to ignore a task-relevant distracter in order to perform efficiently.

A principal component analysis was performed to assess the entire data set described above. One factor accounted for 44% of the total variance in cognitive performance across the six learning tasks. On this same factor, short-term memory duration loaded at a negligible level (0.14), simple span abilities loaded at a moderate level (0.50), and our measure of selective attention loaded heavily (0.78). Given the good separation of simple span and selective attention that we believe these procedures support, these results (consistent with that from the human literature) suggest that simple span and controlled attention may act in unison (but to varying extents) to regulate the relationship between working memory and general cognitive abilities.

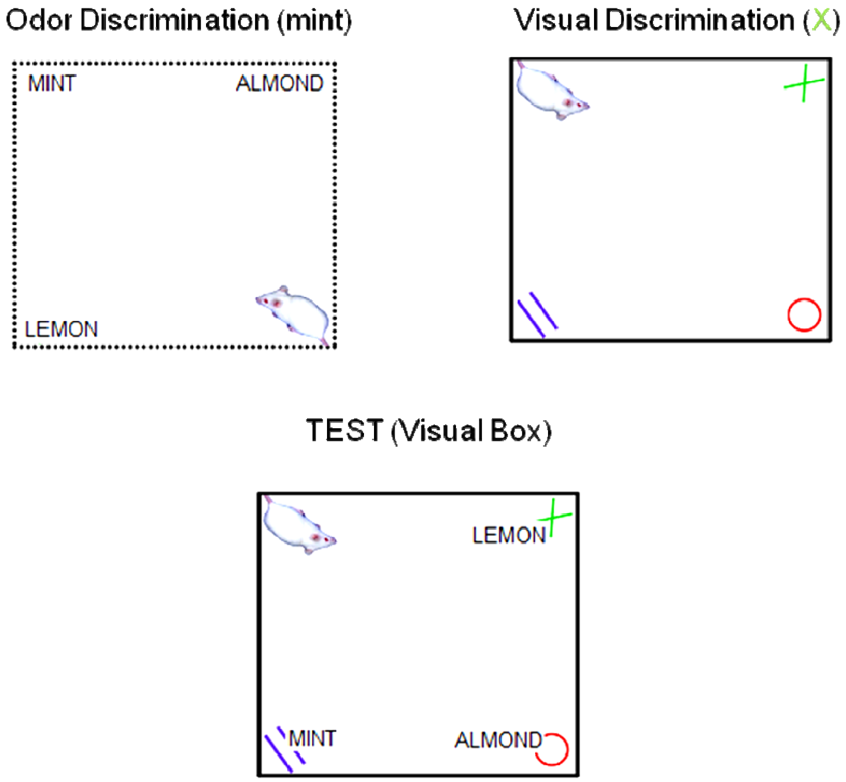


Figure 2. The efficacy of animals' selective attention was assessed in a test analogous to a human Stroop test. In each of two distinct boxes, animals received odor (in the odor discrimination box) or visual (in the visual discrimination box) discrimination training. In the individual tasks (not depicted), the animal could collect food at a location marked by a single discriminative stimulus, e.g., the MINT odor in the odor discrimination box or the green X in the visual discrimination box. (Note that in the actual test, distinct LED arrays served as the visual stimulus). On each trial, the location of the cues was rearranged, but the identity of the target cue remained constant. Mice are quick to learn these discriminations, and will usually attain errorless performance (i.e., they do not approach non-target cues) within four trials. After the completion of training in the simple individual tasks, animals were occasionally tested in the visual discrimination box with odor cues present as salient distracters, or in the odor discrimination box with visual cues present as salient distracters. (These complex discriminations are depicted in the figure above. Note that the target visual and odor cue never appeared in the same location). Unlike the simple discrimination tasks, the presence of salient distracters resulted in an increase in errors (as determined by incorrect choices for the discrimination cue by the test box). Errors in the presence of salient distracters are thought to reflect failures of selective attention, and the number of errors committed by individual animals varied widely. (Adapted from Matzel & Kolata, 2009).

Modulation of Working Memory and General Cognitive Abilities

At least in part, prevailing theory is based on the assumption that the relationship between working memory and intelligence is causal in nature, although by design, the factor analytic techniques that underlie this assertion are correlational. Thus it was of interest to determine whether the observed relationship between aspects of working memory and general cognitive ability were merely correlational or if a causal influence was being revealed by this relationship.

Despite the colloquial (c.f. commercial) contention that “brain exercises” and “smart drugs” can enhance fluid intelligence in normal adults, these claims have rarely been subjected to empirical test, beyond the observation that such treatments have small task-specific benefits. (It is noted that many of the commercial “brain exercise” programs that are marketed to the public make claims of effectiveness based on improvement of performance on a common pre- and post-test of cognitive function, a result that is attributable to a simple practice effect). In fact, decades of rigorous empirical research has found little evidence that environmental variables influence intelligence test performance in any systematic way (Gray et al., 2003). As a simple but compelling example, one of the most “extreme” instances of an environmental manipulation is represented by the process of early-childhood adoption. It has been consistently observed that when a child is removed from the home of low-IQ birth parents, and placed in the home of high-IQ adoptive parents, the IQ of that child as an adult is far more likely to resemble its birth, rather than adoptive, parents (Locurto, 1990; Loehlin, Horn, & Willerman, 1989; Phillips & Fulker, 1989). By comparison, fledgling “brain exercises” are at best trivial (if not unsystematic) manipulations, and thus it is not surprising that they have little influence on intelligence test performance.

Despite our pessimism, we recently questioned whether the general learning abilities of mice could be modulated by extensive training on a task that taxed working memory functions. Light et al. (2010) provided mice with complex working memory “exercise” by training them repeatedly (over a period of weeks) in the dual-radial arm maze task described above (Kolata et al., 2005). This training promoted superior performance when the animals were later tested in our animal analog of the Stroop task, i.e., working memory exercise promoted an improvement in animals’ selective attention. This was not merely an effect of working memory span exercise, as animals that spent comparable time performing in a single eight-arm radial maze did not exhibit the same increase in selective attention performance. Importantly, the animals that had undergone complex working memory exercise exhibited superior aggregate performance in a six-task learning battery. More so than the previous demonstrations of a correlation between working memory capacity/selective attention and general learning abilities, these results suggest the possibility of a causal relationship between the efficacy of working memory and general intelligence. This conclusion is partially supported by the recent report of beneficial effects of complex working memory training on human intelligence test performance (Jaeggi, Buschkuehl, Jonides, &

Perrig, 2008), although this later work has been questioned on methodological grounds (Moody, 2009). However, we must reiterate that intelligence is not likely a unitary phenomenon (Ackerman, 2005; Conway et al., 2003; Heitz et al., 2008), and these results should not be taken to indicate that intelligence and working memory are synonymous, but rather, that working memory may constitute at least some percentage of that trait that we describe as "intelligence." Nevertheless, at the functional level, we are inclined to conclude that working memory training may have at least transient beneficial effects on performance indicative of intelligence.

Our preferred interpretation of the above described relationship between working memory capacity and general learning abilities notwithstanding, those trained in experimental psychology would be quick to point out that "causal relationships" are never as easy to confirm as they are to infer. That said, one might ask if the effect of working memory training on general cognitive abilities is specific, or if the modulation of *any* co-variate with general cognitive abilities might have a similar beneficial impact. Early in our work with mice we observed a consistent positive correlation between various measures of exploration and the aggregate performance of mice on learning test batteries (Matzel et al., 2003, 2006). Various measures of simple *activity* did not bear the same relationship with general learning abilities. We hypothesized that animals of high native exploratory tendencies might make quicker contact with those environmental contingencies upon which learning was based, and thus exploration might *causally* promote general cognitive abilities. We assessed this possibility using a procedure that was conceptually related to the one described above to promote more efficacious selective attention. Here, animals were repeatedly exposed to novel environments, a manipulation that had a long-lasting (at least months, including from pre-pubescence into adulthood) and profound effects on various exploratory behaviors, i.e., exposure to novelty promoted broad increase in exploration. However, this up-regulation of exploratory behaviors had little or no impact on performance on individual measures of learning, and did not promote an increase in the aggregate performance of mice on our learning test batteries (Light et al., 2008). Thus despite the correlation between the propensity for exploration and general learning abilities, and a conceptually logical expectation that a causal relationship might exist between these variables, no such causal relationship could be detected. This set of null results makes the observed relationship between working memory "exercise" and general cognitive performance that much more striking.

The Relationship of General Learning Abilities to Reasoning

As described above, no consensus has emerged regarding the definition of "intelligence." Nevertheless, most definitions (including those provided above) state that intelligent behavior involves the ability to "adapt to the environment" or "learn quickly." These characteristics, like colloquial impressions of intelligence, suggest that learning is a critical component of, if not critically influenced by, intelligence. However, no widely accepted definition of intelligence would begin and end with a statement about the ability to learn. Instead, most definitions make reference to the intelligent beings' capacity to "think rationally," "reason," "engage in reasoning," or colloquially, "to figure out novel solutions" based on limited experience, and the efficacy of reasoning is considered a critical component of cognitive intelligence (Manktelow, 1999). Thus most intelligence test batteries include components specifically intended to characterize an individual's capacity for reasoning. Accordingly, correlations between reasoning and other cognitive tasks (ones not explicitly relegated to the class of reasoning tasks) should co-vary. It is this premise which led us to ask whether animals' general learning abilities were correlated with their capacity for reasoning.

Nominally, the answer to such a question should be well within our grasp. However, much like intelligence, that which constitutes reasoning is not always obvious. Following Aristotle, it is often asserted that reasoning can take one of two forms. In the first, one attempts to understand the "whole" by considering only the component parts. In the second, one attempts to characterize a class of objects by considering the common features of each object in that set. To assess reasoning in laboratory mice, we devised two novel tasks which reflect each of these forms of rational thought. First, animals' performance was assessed in a "decision" or binary tree maze (see Fig. 3). Decision trees are commonly used in operations research, specifically in decision analysis, to identify strategies that are most efficient in reaching a goal. While many search strategies (or paths) could be utilized to visit every node in the decision tree, the vast majority of these paths would lead to an inefficient search, i.e., one which unnecessarily retraces paths or crosses goals that had already been explored. Thus the degree to which an animal can comprehend the whole structure of the maze and implement that information from its current location would be a reflection of a type of reasoning consistent with Aristotle's first description (above).

From a starting location, the decision tree bifurcates (at decision points) into branches. At each decision point is a potential goal location, and the end of each branch terminates in two leaves, each of which also contains potential goal locations, providing a total (in this maze) of 14 potential goals. In our case, the animals' task was to navigate the maze so as to inspect every potential goal for a payoff (in this case, a piece of food).

In the maze illustrated in Figure 3, animals could cross 14 potential goal locations (labeled 1 - 14 in Fig. 3). On a single adaptation day, all goal locations were baited with a food pellet. On subsequent test days (trials), a randomly chosen four- to-eight of the potential goal locations were baited (with the restriction that at least two pieces of food be located on each side of the maze). Thus on any given trial, the animal could not know the location of food or the number of goal locations that were actually baited. It would then be of benefit to the animal to navigate through the decision points in the most efficacious manner possible. Using such a strategy, the animal would pass a maximum of 24 goal locations (as would be required were the animal to search every goal in one half of the maze, efficiently exit that side of the maze, then search every goal in the other half of the maze). What distinguishes this from a maze learning task such as the Lashley Maze is that no single path is "best," i.e., many routes reflect equal efficiency, and an efficient animal will often perform errorlessly across a series of trials, yet will not follow the same route on successive trials. Furthermore, the efficacy with which animals navigate the maze stabilizes very quickly (within 3 - 5 trials), suggesting that animals quickly come to appreciate the underlying structure of the maze, and fix on a strategy for its solution.

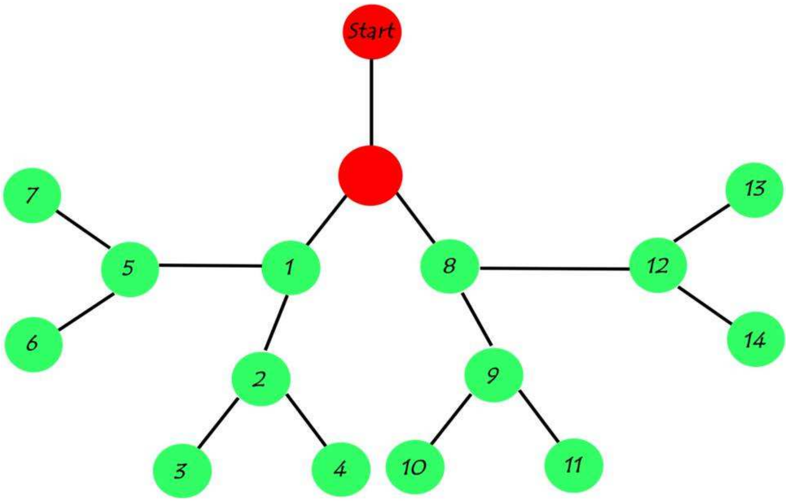


Figure 3. Decision trees (as illustrated above) are commonly used in operations research, specifically in decision analysis, to identify strategies that are most efficient in reaching a goal. While many search patterns (or paths) could be utilized to visit every node in the decision tree, the vast majority of these paths would lead to an inefficient search, i.e., one which unnecessarily retraces paths or crosses goals that had already been explored. Thus the degree to which an animal can comprehend the whole structure of the maze and implement that information from its current location would be a reflection of a type of inductive reasoning. Here, the animals' task was to navigate the maze so as to inspect every potential goal for a payoff (in this case, a piece of food). Animals could cross 14 potential goal locations (labeled 1-14). On test days (trials), a randomly chosen four- to-eight of the potential goal locations were baited (with the restriction that at least two pieces of food be located on each side of the maze). Thus on any given trial, the animal could not know the location of food or the number of goal locations that were actually baited. It would then be of benefit to the animal to navigate through the decision points in the most efficacious manner possible. Using such a strategy, the animal would pass a maximum of 24 goal locations (as would be required were the animal to search every goal in one half of the maze, efficiently exit that side of the maze, then search every goal in the other half of the maze).

Vast amounts of data can be extracted from the performance in this maze, but for the present purposes, a single measure of efficacy is representative of all of the various measures that we have analyzed. To this end, we can simply assess each animal's correct "streak" prior to its unnecessarily crossing a previously crossed goal location, and average the length of this streak across four trials (following 10 trials in which performance is allowed to stabilize). (Note that unlike learning measures, here we assess only animals' *asymptotic* behavior). By this method, perfect performance would be reflected in a streak of 24, wherein all goal locations were explored with maximum efficacy, whereas a streak of less than 24 would reflect less than optimal performance. Thirty one animals were first tested on five learning tasks that constitute our standard learning battery, and were then assessed for performance in the decision tree. When the average streak of individuals was compared to their factor scores (an aggregate measure of performance) extracted from the learning battery test data, a strong correlation (*r*) of 0.60 was observed. To insure that animals did not simply follow a rote path to navigate the maze, on several trials one of the options at one of the second level decision junctions was blocked (thereby disrupting any potential fixed path), and animals' performance on subsequent choices was assessed. Despite this manipulation, the correlation between the animals' average streak and aggregate performance on the learning battery was still strong, $r = 0.51$. This work is presently under review for publication (Wass et al., 2010).

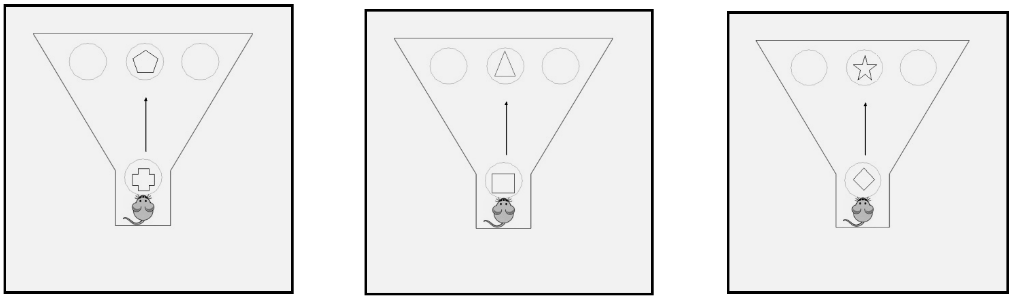
The above data suggests that animals' appreciation of the underlying structure of the decision tree, and their efficient use of this information, co-varies with their general learning abilities. It is noted however, that as a "pure" measure of reasoning, performance in this maze is confounded by short-term memory persistence as well as span (i.e., the animal needs to retain a record of where it has been in order to operate efficiently). Thus although animals' efficient use of structural information could be described as "reasoning," reasoning is not the only potential source of performance variation in this task. Consequently, a second reasoning task based on the concept of "fast mapping" was developed that was not subject to the same caveats. Fast mapping is a mental process whereby a new concept can be learned based on a logical inference derived from a single exposure to limited information. This corresponds with Aristotle's second type of reasoning, i.e., where one attempts to characterize a class of objects by considering the common features of each object in that set.

Fast mapping (Carey & Bartlett, 1978) is believed to play a critical role in the extraordinarily rapid and seemingly effortless acquisition of information during early human development, and explains (in part) the prodigious rate at which children gain vocabulary. For example, when faced with a group of familiar items described by familiar words, an individual will quickly associate an unfamiliar word with a novel item added to the set, and this association requires no overt "pairing" of the novel word and its corresponding novel item. Over time the word's approximate meaning becomes more refined as it is seen in other contexts. Logical inference, as exemplified here, is often asserted to be a hallmark of reasoning.

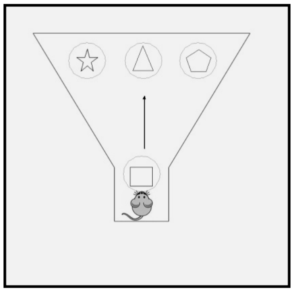
Although extensively studied in humans, few efforts have been made to demonstrate the process of fast mapping in animals, although it has been reported in at least one dog (Tomasello & Kaminski, 2004). It was thus necessary to design a task to assess fast mapping in laboratory mice. The procedure for this task is depicted in Figure 4. For this purpose, animals ($n = 41$) were familiarized with a group of objects (small plastic animals), and were then taught to associate pairs of these objects. This was accomplished by exposing the mouse (while confined to a start box) to one object and then letting the mouse retrieve a piece of food that was hidden under the sample object's paired associate (located in a field adjacent to the start box). For this initial training, the paired associate was the sole object in the test field. After learning a series of such object pairs (much like a word is associated with a meaning), the animals were trained to find the relevant paired associate within a field that contained several objects, all of which had been previously associated with a different sample. This training continued for several weeks until all animals exhibited near errorless choice performance. That is, shown a sample object, they would quickly choose the correct target object from a field of potential choices. After completing this training, animals were occasionally presented with a "fast mapping" test trial. On these trials, animals were exposed to a novel sample object, and then allowed to explore the test field which contained a set of familiar objects (ones that had an established "meaning" based on prior training) and one novel object. The principle of fast mapping suggests that under these conditions, a rational animal should conclude that since the sample object was novel, the food reward should be located under the unfamiliar object in a field of otherwise familiar objects. The number of errors (incorrect choices) that the animals made was averaged across four fast mapping test trials, and these errors were compared to factor scores indicative of each animal's general learning ability (based on performance in the learning test battery). Again, performance on this reasoning task was correlated with animals' aggregate performance in the learning battery, that is, better learners tended to make fewer fast mapping errors, $r(39) = 0.44$, $p < 0.01$. (Wass et al., manuscript under review). It is notable that some animals made *no* fast mapping errors across four trials, a result that, given the number of *potential* errors, is of extremely low probability. This result suggests that fast mapping is well within cognitive repertoire of sub-human animals, including rodents.

In total, the assessment of animals' performance in the binary tree maze and fast mapping task suggests that mice are capable of constructing rational plans and making rational choices. Furthermore, the degree of "rationality" exhibited by individual animals was strongly and consistently correlated with their aggregate performance on a battery of diverse learning tasks.

PHASE 1: Paired Associate Training



PHASE 2: Selection of Familiar Target Object From Familiar Set



TEST: Selection of Novel Target in Otherwise Familiar Set (Fast Mapping)

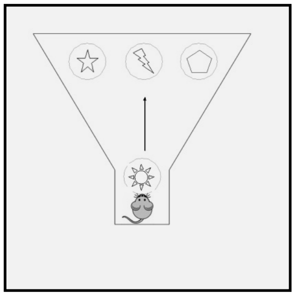


Figure 4. An illustration of the procedure for the "fast mapping" task. Animals were familiarized with a group of objects (small plastic animals), and were then taught to associate pairs of these objects. This was accomplished by exposing the mouse (while confined to a start box) to one object and then letting the mouse retrieve a piece of food that was hidden under the sample object's paired associate (located in a field adjacent to the start box). For this initial training, the paired associate was the sole object in the test field. After learning a series of such object pairs (much like a word is associated with a meaning), the animals were trained to find the relevant paired associate within a field that contained several objects, all of which had been previously associated with a different sample. This training continued for several weeks until all animals exhibited near errorless choice performance. After completing this training, animals were occasionally presented with a "fast mapping" test trial. On these trials, animals were exposed to a novel sample object, and then allowed to explore the test field which contained a set of familiar objects (ones that had an established "meaning" based on prior training) and one novel object. The principle of fast mapping suggests that under these conditions, a rational animal should conclude that since the sample object was novel, the food reward should be located under the unfamiliar object in a field of otherwise familiar objects. (Note: For simplicity, the directional arrows illustrated above all point to a correct target object located in the center position of the test field. During actual tests, the location of the correct target was randomly determined on each trial).

Summary

The results summarized above suggest that the general learning abilities, selective attention, and reasoning capacity of genetically heterogeneous mice are commonly regulated. To return to one of the definitions of intelligence provided above, concepts of "intelligence" are attempts to classify "the ability to understand complex ideas, to adapt effectively to the environment, to learn from experience, to engage in various forms of reasoning, to overcome obstacles by taking thought." While this and other similar definitions were conceived to account for human behavior, this same definition appears relevant in summarizing the performance of mice on this diverse set of cognitive tasks. Thus like humans, mice appear to express individual variations in intelligence, and these variations have profound functional consequences for the animals' negotiation of their environments.

It is important to note that the work reviewed above was originally conceived as a method to assess individual variations in the general *learning* abilities of mice, and was not intended to assess "intelligence" or the conservation of this trait across humans and mice. However, in several published commentaries on our initial studies, it was noted that what we described as variations in general learning ability would in other contexts be described as a reflection variations in intelligence (Blinkhorn, 2003; Chin, 2003). It is in this regard that we have attempted to establish an analogy between the concepts of intelligence in humans and mice. This attempt is far from straight-forward, given the difficulties that are posed by any attempt to define intelligence (see above). Nevertheless, as a starting point, the co-variation of broad learning capabilities, attentional abilities, and the capacity for various forms of reasoning, is suggestive of a conservation of the cognitive trait that is at least colloquially described as "intelligence."

Certain principles have emerged from these studies with animals. These conclusions have been consistent with many of those derived from human research, and in some instances, have allowed conclusions that go beyond that which could be derived from studies of humans. First, we have observed that the parameters of both storage and processing components of a system analogous to working memory are correlated with animals aggregate performance on a battery of behavioral tests designed to assess a range of learning abilities. Although working memory capacity (or resistance to interference) was a more consistent and reliable predictor of general cognitive abilities than was simple span or resistance to decay, these storage components of working memory do have some predictive validity, and their predictive abilities appear to increase as a function of the degree to which they are taxed (as is necessarily the case with aged animals; see Matzel et al., 2008). Thus we have concluded that both storage and processing aspects of the working memory system may play a role in the establishment of individual differences in higher cognitive abilities, depending on task demands and the nature of the test. This conclusion is similar to that which has emerged from studies with humans (Halford, Cowan, & Andrews, 2007; Unsworth & Engle, 2007). It has been suggested that the role of the storage and processing components of working memory in the establishment of higher cognitive abilities may arise from their common reliance on (and limitations of) attention (Cowan et al., 2006). As Cowan et al. have enumerated, it is often difficult to separate these processes in tests of humans owing to their reliance on mnemonic strategies such as rehearsal and grouping. These strategies (particularly those reliant on verbal processing) are at least partially mitigated with animal subjects. In this regard, it is notable that the performance of mice on an analog of the Stroop test (in which the animals must focus on a target stimulus against a background of relevant distracters) was highly correlated with aggregate performance on a learning test battery. Since there is no obvious storage requirement for efficient performance on this task, this result suggests that processing aspects of working memory (i.e., selective attention) may have at least some unique relationship to the expression of higher cognitive abilities. Relatedly, we have determined that manipulations (e.g., working memory "exercise") that promote the more efficacious utilization of selective attention have commensurate effects on general cognitive performance, suggestive of a causal relationship between these variables.

In total, available data suggests a conservation of the structure and determinants of "intelligence" in both human and non-human animals. The qualitative correspondence of the concept of intelligence in humans and infra-human animals provides the opportunity for complimentary lines of research, and animals provide a practical opportunity to address lines of inquiry that are not always tractable in humans (e.g., Kolata, Light, & Matzel, 2008). To this end, Kolata, Light, Wass, Sahil, and Matzel (2009) have now quantified the RNA transcripts of approximately 25,000 known genes in several limited brain regions (including the prefrontal cortex) of animals classified as expressing high or low general cognitive abilities. As this work is presently under review, it would be premature to provide a detailed description of these results here. However, our analyses indicate a specific co-variation between a set of genes related to dopamine signaling in the prefrontal cortex and the aggregate performance of animals in the learning battery. It is of course notable that computational modeling has implicated dopaminergic connectivity in the prefrontal cortex to working memory (Durstewitz, Seamans, & Sejnowski, 2000a, 2000b), and these conclusions have been supported by empirical observations (Meyer-Lindenberg et al., 2007); for review, see (Matzel & Kolata, 2010). As the results of Kolata et al. (2010) are based on RNA transcripts, analogous work is presently intractable in human subjects. Thus in combination with human work, studies with animals may provide insights into what Jensen (1998) has described as the "holy grail" of intelligence research, i.e., the biological basis for this ubiquitously manifest cognitive trait and its role in the establishment of individual differences in intelligence.

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