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Journal of Neuroscience Methods 146 (2005) 165–173

NEUROSCIENCE METHODS

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A non-human primate test of abstraction and set shifting: An automated adaptation of the Wisconsin Card Sorting Test

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Received 18 November 2004; received in revised form 11 February 2005; accepted 14 February 2005

Abstract

Functional assessment of the prefrontal cortices in the non-human primate began with the seminal work of Jacobsen in the 1930s. However, despite nearly 70 years of research, the precise nature of the cognitive function of this region remains unclear. One factor that has limited progress in this endeavor has been the lack of behavioral tasks that parallel most closely those used with humans. In the present study, we describe a test for the non-human primate that was adapted from the Wisconsin Card Sorting Task (WCST), perhaps the most widely used test of prefrontal cognitive function in humans. Our adaptation of this task, the Conceptual Set-Shifting Task (CSST), uses learning criteria and stimuli nearly identical to those of the WCST. The CSST requires the animal to initially form a concept by establishing a pattern of responding to a given stimulus class, maintain responding to that stimulus class, and then shift to a different stimulus class when the reward contingency changes. The data presented here establishes baseline performance on the CSST for young adult rhesus monkeys and demonstrates that components of prefrontal cognitive function can be effectively assessed in the non-human primate in a manner that parallels the clinical assessment of humans.

Keywords: Rhesus monkey; Executive function; Prefrontal cortex; Wisconsin Card Sorting Test

1. Introduction

Assessment of the cognitive functions of the prefrontal cortex (PFC) in the non-human primate began with the seminal work of several researchers in the early 1920s and 1930s (Jacobsen, 1935, 1936; Bianchi, 1922; Breslau et al., 1994). They demonstrated that lesions in the PFC impair performance on cognitive tasks, such as delayed response and delayed alteration, tasks that are now thought to require "working memory", a short-term buffer for "working with" recently presented and remembered stimuli (Baddeley, 1986). More recent work in the field, using a variety of tests with non-human primates, has implicated the prefrontal cortices (i.e., all those regions rostral to the motor and premotor cortices) in learning, memory and executive function (Dias et al., 1996; Roberts et al., 1994; Gaffan and Harrison, 1989; Bachevalier and Mishkin, 1986; Woods and Knight, 1986; Passingham, 1985; Mishkin and Manning, 1978; Oscar-Berman, 1978; Rosen et al., 1975; Pohl, 1973; Butters and Pandya, 1969). Examples of tests include, the delayed response test, the delayed alternations test, the reversal-learning test and a test of attentional set shifting (Roberts et al., 1988; Dias et al., 1996; Diamond, 1990; Goldman et al., 1971; Pohl, 1973). Animals with damage to the prefrontal regions have been shown to be impaired on these tests (i.e., Jacobsen: delayed response test; Pohl: reversal learning). However, despite nearly 70 years of research, the precise

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doi:10.1016/j.jneumeth.2005.02.005

nature of the cognitive function subserved by this region remains unclear. One factor that has limited more rapid progress in this endeavor has been the lack of behavioral tasks that parallel more closely those used with humans.

In humans, the Wisconsin Card Sorting Test (WCST; Grant and Berg, 1948) is the most frequently employed instrument used to assess prefrontal cortex function (Berg, 1948; Milner, 1968, 1995). The WCST assesses the ability to abstract, maintain, and shift cognitive set according to changing reward contingencies (Nagahama et al., 1996; Damasio and Anderson, 1993; Heaton et al., 1993). Essential components of the WCST paradigm have been incorporated into a task developed for non-human primates by Roberts et al. (1988). The task assesses both extra-dimensional and intra-dimensional shifting of set, but does not use the same stimuli as that of the WCST. Our adaptation of the WCST for the non-human primate, the Conceptual Set-Shifting Task (CSST), uses the same basic principles, learning criteria, as well as the identical stimuli as those of the WCST. The CSST requires the animal to initially form a concept by establishing a pattern of responding to a given stimulus class (color or shape), maintain responding to that same stimulus class, and then shift to a different stimulus class when the reward contingency is changed. The data presented below establishes a baseline performance on the CSST for young adult rhesus monkeys and demonstrates that components of prefrontal cognitive function can be effectively assessed in the non-human primate in a manner that parallels closely those used in the clinical assessment of humans.

2. Materials and methods

2.1. Subjects

The behavioral data in this study was obtained from eight young adult male rhesus monkeys (*Macaca mulatta*) that served as normal controls in our ongoing behavioral studies of normal aging (Moore et al., 2003). All of the monkeys described in this report were obtained from the Yerkes National Primate Research Center and had known birth dates and complete health records. Prerequisite to entering the study, each monkey received a complete medical examination and explicit exclusion criteria were applied for the following conditions: splenectomy, thymectomy, exposure to radiation, cancer, organ transplantation, malnutrition, chronic illness including viral or parasitic infections, neurological diseases, or chronic drug administration. All of the monkeys were individually housed and were in constant auditory and visual range of other monkeys. Monkeys were fed a diet of Purina Chow and fruit at the end of testing each day and on weekends. Water was available continuously. The monkeys were maintained under a 12-h light/dark cycle that changed gradually over the course of an hour. All animals were checked daily by animal technicians for health and well-being and were given a medical exam by staff veterinarians every 6 months. The monkeys used in the present study were behaviorally sophisticated. Each had been tested on the Delayed Non-Matching to Sample (DNMS), both acquisition of this task and delays of 2–10 min as well as the Delayed Recognition Span Test (DRST) prior to the administration of the CSST. The details of the DNMS and DRST tasks are described elsewhere (Herndon et al., 1997; Moss et al., 1997).

2.2. Apparatus

On testing days, animals were transferred from their home cage into a mobile testing cage approximately 36 in. square × 50 in. height. One side was double-walled so that the outer small mesh side could be removed exposing a larger grid with square openings 3 in. × 3 in. on a side that allowed the monkey to easily reach out of the testing cage. The mobile cage was moved into a sound-attenuating chamber that contained a 19 in. touch-sensitive and resistive computer screen controlled by a Macintosh-based computer. For stimulus presentation, the computer screen was divided into a 3 × 3 matrix (unmarked). Rewards of M&Ms or Skittles candies were delivered from an automated dispenser (Med Associates) by a tube into a tray located immediately beneath the touch screen. The interior of the testing chamber was darkened and the apparatus was located in a darkened room. White noise was presented through two speakers, one mounted on each side within the automated apparatus to mask extraneous sounds. Stimulus presentation, touch screen monitoring and reward delivery were controlled by a behavioral testing program, "Glyph", which was developed for assessing cognitive functions in mentally challenged adults and children. A non-correctional procedure was used throughout testing.

2.3. Behavioral testing

Testing consisted of three tasks administered in the following order: a pre-training task to adapt the monkey to the touch screen, a three-choice discrimination to assess the monkeys ability to respond to stimuli of the type to be used in the CSST, and the CSST task that consists of an initial abstraction and three subsequent shifts of stimulus set.

2.4. Automated pre-training

The automated pre-training task was used simply to teach each monkey to touch the computer screen. This task required the monkey to touch a single stimulus that appeared in a pseudorandom fashion in one of the nine locations on the screen. The stimulus was an image of an apple that was left on the screen for 60 s or until the monkey touched it. The inter-trial interval was 15 s. Touching the stimulus delivered a food reward into the tray beneath the screen. The animals were initially rewarded for touching any portion of the screen, and then were subsequently shaped to touching only the apple stimulus. Pre-training was administered for 20 trials a day until the monkey correctly responded to all 20 consecutive trials in a single day. The day after the monkey completed the pre-training task, they began a simple three-choice discrimination task.

2.5. Three-choice discrimination task

This task was administered to establish that monkeys could discriminate among three fixed stimuli that differed in shape and color, but were not identical to those that would be used in the CSST. As shown in Fig. 1, the task presented the monkey with a pink square, an orange cross, and a brown 12-point star on each trial. The stimuli remained constant in terms of color and shape for each trial while their spatial location among the nine screen positions was varied from trial to trial in a pseudorandom sequence that was balanced over 4 days of testing. The pink square was the positive stimulus for all trials and a non-correctional procedure was used throughout this task. The stimuli remained on the screen for 60 s. The inter-trial interval was 15 s. Testing was administered for 80 trials per day until the monkey chose the pink square on 10 consecutive trials during one testing session to reach the criterion level of performance. The discrimination task was only available to be given to a subset of monkeys. However, an analysis of the data comparing the performance of the monkeys who had completed the discrimination task to those that did not suggest that experience on this task did not significantly alter performance on the CSST.

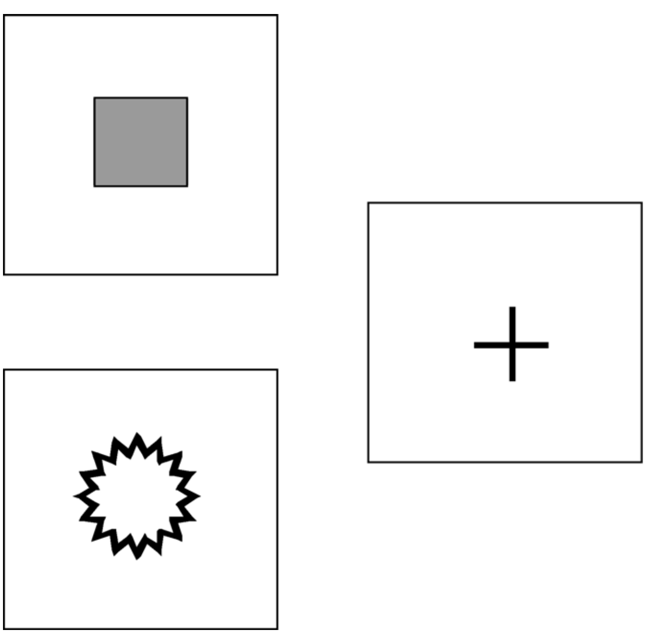

Fig. 1. Schematic of a single trial of the discrimination task. On each trial the monkey is presented with three stimuli: a pink square, an orange cross and a brown 12-point star. The correct response on all trials is the pink square. The monkey must choose this stimulus on 10 consecutive trials in order to reach criterion. Once criterion is reached, testing is started the next day on the CSST (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.).

2.6. Conceptual set shifting task

Formal testing began on the CSST on the day following the completion of the pre-training or discrimination tasks. As shown in Fig. 2, the stimuli for the CSST differed in two relevant dimensions, color (red, green, or blue) and shape (triangle, star, and circle). All nine possible combinations of stimuli (i.e., red triangle, red star, red circle, blue triangle, etc.) were presented in four pseudorandom sequences to the monkeys over 4 days of testing. If the monkey did not make criterion on the 4th day of testing, the same four sequences of trials was administered in the same order until criterion was reached. This procedure ensured that stimuli dimensions and locations were presented in a balanced randomized fashion. On each trial, three different stimuli were presented representing all three colors and all three shapes as indicated in Fig. 2. On each trial, the three stimuli were presented in a pseudorandom order in three of nine locations on the computer touch screen (Fig. 2). If a monkey did not respond to the touch screen within 60 s, the screen reverted to blank, a non-response was recorded and the inter-trial interval began. For all trials, the inter-trial interval was 15 s during which the screen was blank. Each day of testing consisted of 80 trials.

All monkeys were tested sequentially on four phases of the CSST: initial abstraction (red), shift-1 (triangle), shift-2 (blue) and shift-3 (star). During the initial abstraction and acquisition of the first conceptual set, the monkey had to choose the red stimulus regardless of its shape in order to obtain a food reward. Once the monkey chose this stimulus on 10 consecutive trials, the program switched the rewarded contingency during the same testing session without alerting the monkey. Thus, the monkey now had to choose the triangle stimulus, regardless of its color to obtain a food reward. In all phases of the test, once the monkey reached a criterion of 10 consecutive correct responses, the remaining trials for that day rewarded the new concept so that intra-day data on the shift could be obtained.

Testing then continued on the new stimulus contingency until the monkey again reached a criterion of 10 consecutive responses. The computer then switched the rewarded contingency to the color blue, regardless of its shape. Finally, when criterion was reached on the blue category, the contingency was switched to the last category star. Testing continued on this category until criterion was reached.

For the automated pre-training task, the number of trials to criterion and non-responses were recorded. For the three-choice discrimination, the total number of trials, errors, and non-responses to criterion were recorded. For the CSST, the total number of trials and errors to criterion for the red condition were recorded, while for the subsequent three shift conditions, the total number of trials, errors, and perseverative errors were recorded. In addition, the total number of broken sets, perseverative errors and non-responses made across all three shifts and the perseverative errors as a percent of total shift trials (sum total of trials during the shift conditions) were determined.

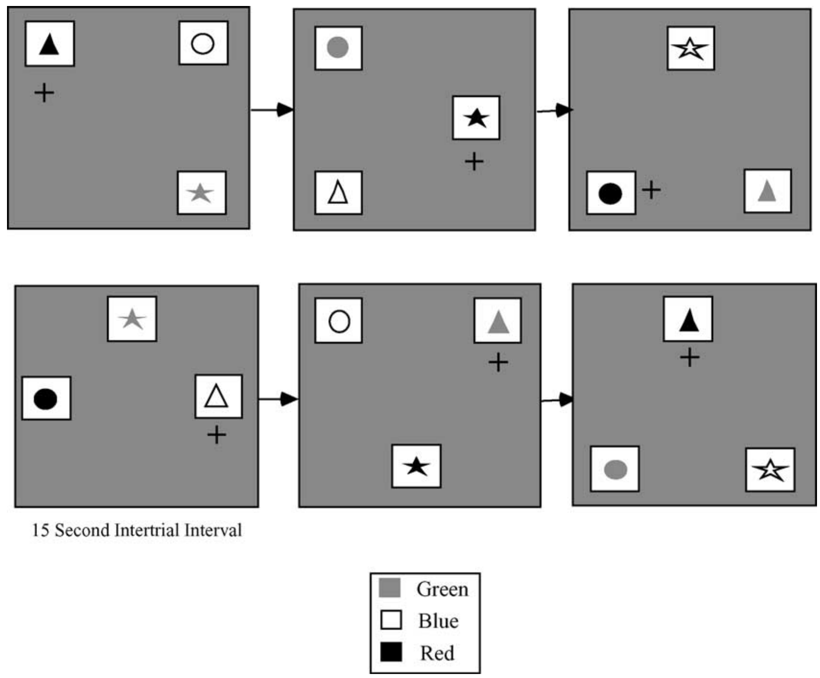

Fig. 2. In this schematic of the Conceptual Set Shifting Task (CSST), each screen (panel) represents one trial. On each trial, the monkey is presented with three stimuli that vary in shape and color. During the first concept condition, the monkey must choose the red stimulus regardless of its shape as illustrated in the top three screens. Once the monkey chooses the correct stimulus on 10 consecutive trials, the computer switches the rewarded stimulus on the same testing day, without alerting the monkey. In the second concept condition, the monkey must chose the triangle-shaped stimulus, regardless of the color, as illustrated in the bottom three screens. Again, when the monkey chooses the correct stimulus for 10 consecutive trials the computer switches the rewarded stimulus on the same testing day, without alerting the monkey. Testing is continued in this same manner for the blue and star conditions (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.).

A perseverative error was recorded when a monkey made an error by choosing a stimulus that contained the component of the previously rewarded concept. A broken set was recorded when a monkey achieved a span of six–nine consecutive correct responses, but then made an error and missed reaching criterion of 10 straight correct responses. A non-response was recorded when a monkey failed to respond by touching the screen on any trial within 1 min of the stimuli appearing on the screen. A non-response was not counted as an error, but it did reset the count of consecutive correct responses to zero (i.e., for purposes of achieving criterion performance). Thus, the total number of trials and errors did not include the number of non-responses.

3. Results

All results are analyzed with standard parametric statistics including one-way and two-way analysis of variance (ANOVA). Post hoc paired comparisons were evaluated using the Bonferroni correction to protect against inflation of Type 1 error.

3.1. Pre-training task

Monkeys differed dramatically in the ease with which they mastered touching the computer screen in this pre-training task. Trials to criterion ranged from 60 to 300. However, there were no indications that the number of trials required to learn this task was, in any way, related to subsequent performance.

3.2. Three-choice discrimination task

Table 1 shows the performance of the monkeys on the initial three choice discrimination task in terms of trials, errors and non-responses to criterion.

The discrimination task was only available to be given to a subset of monkeys. However, a one-way ANOVA comparing the performance of the monkeys who had the discrimination

Table 1
Trials and errors, and non-responses for each monkey on the discrimination task

Monkey	Trials	Errors	Non-responses
AM 092	193	55	14
AM 093	N/A	N/A	N/A
AM 094	188	95	0
AM 095	201	97	12
AM 128	142	68	0
AM 132	177	65	3
AM 163	378	210	27
AM 202	137	52	0
Mean	202.29	91.71	8.00
S.E.	28.47	19.29	3.59

N/A: Indicates monkeys that were not given this task; S.E. = standard error.

Table 2
Trials and errors for each monkey on the initial abstraction of the CSST

Monkey	Trials	Errors
AM 092	87	36
AM 093	160	72
AM 094	116	58
AM 095	147	76
AM 128	185	69
AM 132	131	55
AM 163	129	66
AM 202	141	58
Mean	137.00	61.25
S.E.	9.67	4.17

S.E. = standard error.

task to those that did not was completed, and the data suggested that experience on this task did not significantly alter performance on the CSST.

3.3. Conceptual set shifting task (CSST)—initial abstraction

Table 2 shows the monkeys performance on the initial abstraction of the first concept (red).

3.4. Conceptual set shifting task (CSST)—shifts 1, 2 and 3

Tables 3–5 show the performance of the monkeys on the three subsequent shift conditions (triangle, blue and star).

One particularly important measure in regards to PFC function is the tendency to perseverate in response pattern during the shift conditions. This aspect of PFC function was assessed in several ways. First, the total number of perseverative errors (when a monkey made an error by choosing a stimulus that contained the component of the previously rewarded concept) was determined (Table 6). Then, since it is plausible that as the number of trials required to reach criterion increased so does the number of opportunities to make a perseverative error, we further analyzed this type of error by calculating the total perseverative errors as a percentage of total shift trials (Table 6).

Table 3
Trials, errors, and perseverative errors for each monkey on the first shift of the CSST

Monkey	Trials	Errors	PE
AM 092	252	120	55
AM 093	297	175	43
AM 094	257	132	49
AM 095	318	162	90
AM 128	352	178	133
AM 132	221	108	58
AM 163	153	91	60
AM 202	398	228	187
Mean	281.00	149.25	84.38
S.E.	25.54	14.84	16.79

S.E. = standard error.

Table 4
Trials, errors, and perseverative errors for each monkey on the second shift of the CSST

Monkey	Trials	Errors	PE
AM 092	187	94	77
AM 093	223	104	78
AM 094	179	115	40
AM 095	195	107	89
AM 128	163	111	81
AM 132	219	120	81
AM 163	290	143	106
AM 202	400	234	168
Mean	232.00	128.5	89.88
S.E.	25.86	14.87	12.08

SE = standard error.

Table 5
Trials, errors, and perseverative errors for each monkey on the third shift of the CSST

Monkey	Trials	Errors	PE
AM 092	187	84	55
AM 093	174	97	69
AM 094	228	137	55
AM 095	337	158	64
AM 128	336	186	104
AM 132	226	120	82
AM 163	256	109	64
AM 202	327	190	144
Mean	259.90	135.10	79.63
S.E.	22.05	13.17	10.12

S.E. = standard error.

Table 7 shows the total of number of broken sets and non-responses for each monkey. Broken sets is a measure of maintaining a response pattern based on reinforcement contingencies, whereas non-responses may represent a temporary change in response pattern due to increased task difficulty during the shift conditions since no non-responses were observed during the discrimination task (a relatively simpler task than the CSST).

Table 6
Total perseverative errors across all shift conditions and total perseverative errors as a percent of shift trials for each monkey on the CSST

Monkey	PE	PE as a percent of shift trials
AM 092	187	29.87
AM 093	189	27.23
AM 094	144	21.69
AM 095	243	28.59
AM 128	318	37.37
AM 132	221	33.18
AM 163	230	32.90
AM 202	499	44.36
Mean	253.88	31.90
S.E.	36.81	2.27

S.E. = standard error.

Table 7
Total number of broken sets and non-responses for each monkey on the CSST

Monkey	BS	NR
AM 092	16	1
AM 093	10	12
AM 094	12	174
AM 095	4	5
AM 128	8	75
AM 132	6	28
AM 163	12	69
AM 202	8	10
Mean	9.50	46.75
S.E.	1.26	19.46

S.E. = standard error.

4. Discussion

The Conceptual Set Shifting Task (CSST) is a task that was adapted from and parallels closely the Wisconsin Card Sort Task (WCST), a task used for over 50 years for the assessment of "higher cortical" function in humans (Grant and Berg, 1948; Berg, 1948; Milner, 1968, 1995). The present study documents the feasibility of adapting the principles of the WCST and applying them through a task designed for use with the monkey to assess components of PFC cognitive function. A detailed discussion of the CSST paradigm, as well as outcome measures, patterns of performance observed on the task, and analyses of errors follow in two separate sections below. These two sections are followed by a brief discussion of the WCST and CSST as measures of PFC function.

4.1. The CSST paradigm

4.1.1. Three-choice discrimination

For the three-choice discrimination task, three stimuli, each of which differs from the other two in color and shape, are presented simultaneously on the touch screen. Position is randomized and selection of the designated positive stimulus is followed immediately by delivery of a reward. The remaining two stimuli are designated as negative, and selection of either of these is followed by non-reward and blacking out of the screen. Hence, the monkey is required to always select the positive stimulus and establish this stimulus–response association to a consistent, high level of accuracy. As a pre-training/control task, the three-choice discrimination achieves several goals that are requisite to perform the CSST task. First, it familiarizes the monkey with the mode of stimulus presentation. Second, it ensures the animal's ability to discriminate among three stimuli along the dimensions that will be used throughout the task, and third, it establishes that the animal can maintain a high-level of accuracy for a given reward contingency. As such, the three-choice discrimination should always be administered as prerequisite to the initial abstraction and set-shifting components of the CSST.

4.1.2. Initial abstraction

On the initial abstraction of the CSST, stimuli composed of all combinations of the three colors and three shapes (all different from those used for the three-choice discrimination) comprise the set of nine different stimuli that are used throughout the task. From this set, three different stimuli are presented on each trial, such that each of the three shapes and each of the three colors is always present. In this phase of the CSST, the animal learns the rule that the relevant dimension is color, and not shape, by rewarding the animal for choosing the red stimulus in each trial regardless of its shape. Achieving a high degree of accuracy on this phase of the task (typically within a range of 60–160 trials) can be interpreted as evidence of the animal's capacity to abstract a concept based on a singular dimensional feature of the stimulus. It is clear that learning this phase is required in order to continue to the next phase of the task, in which the animal's capacity to shift from an established and learned dimensional set to a newly designated and previously unlearned set is assessed.

4.1.3. Shifts of set

Once the monkey has learned the initial dimension (color) and stimulus (red) in the abstraction phase of the task, the reward contingency is changed to a different dimension, shape (in this initial instance with triangle as the correct stimulus). The animal must now form a new dimension–reward association while "unlearning" or inhibiting the formerly learned dimension–reward association. Not surprisingly, learning of this shift requires a significantly greater number of trials than for the initial abstraction (mean of 103 trials versus 248 trials, respectively), which likely reflects the combined processes of the "unlearning" and new learning on this task. Two subsequent shifts in dimension (blue and then star) are then administered, each to the same learning criterion as that in the previous two stages. The mean trials required to learn these two subsequent shifts appears to be lower than that of the initial shift (143 trials and 185 trials, respectively) and suggests that animals may be evidencing "learning to learn" the shifting strategy. This is an empirical question that could be directly addressed by further extending the number of dimensional shifts on the task. This is an interesting, but separate issue that awaits future investigation.

4.1.4. Related tasks employing "shift of set"

It may be of interest to compare the CSST to other behavioral tasks that have been used in the field to assess the ability to change a learned "strategy" in the face of a changing reinforcement contingency (i.e., shift of set). One of the first, and perhaps most classic, tasks of this type was the delayed spatial alternation task (Jacobsen, 1935) in which the animal is required to alternate responses from a rewarded stimulus located to the left side of the animal to a rewarded identical stimulus located to the right of the animal. This task has also been used in a non-spatial form in which the animal must alternate responses between two different stimulus objects, where the spatial location is changed from left to right in a random fashion to preclude the use of spatial cues to solve the task. A related form of delayed alternation task is the discrimination reversal task that can also be administered in a spatial and non-spatial form. For reversal learning, the animal is first taught to respond reliably to one of two objects (or to either left or right locations) and, after reaching a specified learning criterion, the reinforcement contingency is changed to now reinforce the other object (or location). The initial reversal is then followed by additional reversals (typically three or greater) or until the animal can "reverse" within the same session without error (Mahut, 1971; Jones and Mishkin, 1972; Lai et al., 1995). The delayed alternation and discrimination reversal tasks in either their spatial or non-spatial forms require the animal to shift within a dimension rather than shifting to another previously irrelevant dimension. It might be argued that the intra-dimensional shifts (e.g. shifting from color to color) required in alternation and reversal tasks make different, and perhaps less complex, demands than those requiring extra-dimensional shifts (e.g. shifting from color to shape) as on the WCST and CSST.

A more complex task of frontal lobe function, and another analogue of the WCST, was developed in England for use with the non-human primate (Roberts et al., 1994; Dias et al., 1996; Robbins et al., 1996). This task is a visual discrimination paradigm that requires intra-dimensional and extra-dimensional shifts that assess attentional set in both humans and non-human primates (Roberts et al., 1988). Compound stimuli comprised of colored shapes and black lines are used in this task and subjects are required to maintain an attentional set, shift their attentional set within the same perceptual dimension (intra-dimensional shift) and shift their attentional set from one perceptual dimension to another (extra-dimensional shift) (Roberts et al., 1988; Dias et al., 1996). Testing consists of simple and compound discriminations, intra-dimensional and extra-dimensional shifts, probe tests and reversals and it has been administered on an automated apparatus and a hand-testing apparatus (Roberts et al., 1988; Dias et al., 1996). While this test is comparable to the WCST, it does differ in several aspects. First, the stimuli used in the attentional set-shifting task are markedly different from those used in the WCST and differ across trials, whereas the CSST was developed to be a direct analogue of the human WCST by using the basic principles, learning criterion and similar stimuli of the WCST. Second, the inclusion of an intra-dimensional shift provides further information regarding maintenance of set; however, the intra-dimensional shifts are difficult to distinguish from learning new complex discriminations. Though this type of shift is important, it is not currently measured in the WCST or CSST. However, the CSST could be easily modified to include intra-dimensional shifts (shifting from one color to a second color) without changing the nature of the task.

Roberts et al. (1988), using their attentional set-shifting task, have repeatedly demonstrated that performance on an intra-dimensional shift is superior to performance on an extra-dimensional shift. In addition, they have used this task extensively in studies investigating the effects of lesions in the PFC. For example performance by marmosets with excitotoxic lesions of the lateral (Broadman Area 9) and orbital (Broadman Areas 11, 12 and 13) PFC regions was equivalent to controls on intra-dimensional shifts but was impaired relative to controls on extra-dimensional shifts (Dias et al., 1996). These findings are comparable to the performance by a group of rhesus monkeys tested with the CSST. These animals had bilateral lesions of the prefrontal cortices, including Brodmann areas 46, 9 and 10, and their performance was characterized by impaired abstraction and set shifting on the CSST (Moore et al., 2001).

4.2. Outcome measures, patterns of performance and error analyses

4.2.1. Outcome measures

The CSST offers several measures that can be used to characterize performance on the task for both the abstraction and set-shifting phases. The standard measures of trials and errors required to reach learning criterion on the initial abstraction phase provides a basic index of the overall rate of learning. The same two outcomes can be applied to each of the three-shift phases. In addition, the total number of broken sets, perseverative errors and non-responses made across all three shifts and the perseverative errors as a percent of total shift trials (sum total of trials during the shift conditions) can be determined.

A Pearson's correlational matrix was used to determine if these variables were independent measures. The analysis revealed no significant relationship amongst these variables, therefore, demonstrating that each variable is an independent measure. Patterns of performance based on these variables provide insight into cognitive processes, such as abstraction, set shifting and inhibition of perseverative responses, all of which are thought to be mediated in part by the PFC (Milner, 1995; Omori et al., 1999; Petrides, 2000a,b; Robbins, 1996; Stuss and Benson, 1986).

4.2.2. Patterns of performance

With the use of additional shifts, one can be in a position to determine the rate at which animals can "learn how to learn" dimensional shifts. By example, can monkeys learn to perform a shift after the first or second trial that the reward contingency is changed to a different dimension? Alternatively, will monkeys under certain experimental conditions of manipulations show a steady level of shift-to-shift performance, but never evidence improvement over shifts? It is plausible that in some instances (e.g. selective reversible lesions), one might uncover whether animals demonstrate superior performance in shifting set to one particular dimensional domain as compared to others.

4.3. Analyses of errors

4.3.1. Perseveration

Shifts of dimensional set require not only the acquisition of a new stimulus–response association, but also the suppression of previously rewarded relationships. As a consequence, they provide an opportunity to assess the number of trials required and errors committed to successfully achieve this transition. Errors committed following a shift in reward contingencies that involve choosing a stimuli that contains the component of the previously rewarded concept, particularly when they exceed the level expected by that in a "normal" control or reference group, have been identified as "perseverative" responses or, more generally, as perseverative behavior. In the extreme, perseveration manifests itself as a behavior in which the patient or animal is unable to successfully shift to the new reward and relentlessly continues to respond to the previously correct stimulus dimension in the absence of reward. For the CSST, as described in the methods section above, perseveration can be assessed with different scoring criteria. First, one can measure the total number of perseverative errors across all shift trials. But since it is plausible that the number of opportunities to make a perseverative error increases as the number of trials required to reach criterion increases, one can refine this measure of this type of error by calculating the total perseverative errors as a percentage of total shift trials. Finally, the number of perseverative errors expressed as a percent of total errors (errors made to stimuli that were not rewarded in the current or previously correct dimensional set) provides the opportunity to assess if the number of perseverative errors committed significantly exceeds that expected due to chance.

4.4. The WCST and CSST as measures of prefrontal cortical functions

Successful performance on the WCST has been convincingly shown throughout the human literature to be dependent on the cognitive functions mediated by the prefrontal cortices (Milner et al., 1968; Milner, 1995; Roberts et al., 1994; Stuss and Benson, 1986). The use of the CSST in monkeys has begun to reveal a similar relationship. A preliminary study in monkeys with bilateral lesions of the prefrontal cortices, including Brodmann areas 46, 9 and 10, reveal an impairment on the abstraction and shifting stages of the CSST (Moore et al., 2001). Deficits on the CSST have also been described as one of the primary cognitive deficits observed in a non-human primate model of hypertension (Moore et al., 2002) in the aged monkey (Moore et al., 2003), and appears to represent one of the first cognitive domains to evidence impairment in middle age (Moss et al., 2003; Moore et al., in preparation).

4.4.1. Conclusions

The present report provides data obtained from a group of young adult rhesus monkeys on a test of executive function that parallels closely a human neuropsychological test that has been used for the past >50 years. A detailed description of the administration and behavioral components of the task, as well as a discussion of the patterns of performance observed and analyses of errors amenable to the task are also provided Together, they demonstrate that the CSST is a suitable task that can assess several components of executive function, specifically abstraction, set-shifting and response suppression, in the non-human primate in a manner that parallels methods used in the clinical assessment of humans.

Acknowledgments

This research was supported by NIH grants P01-AG00001, R37-AG17609 and RR00165. The authors wish to thank Sarah Hix, Beverly Duryea-Steiger and Dana Whitelaw for their valuable assistance with this project. The authors also wish to thank Ben Wallace at the Eunice Kennedy Shriver Center for the Glyph software we used to implement the Conceptual Set Shifting Task.

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