11 The Cambridge Neuropsychological Test Automated Battery in the Assessment of Executive Functioning

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Computerized administration of clinical instruments is not an entirely new phenomenon. The first personal computers were introduced into wide use in the 1970s. Rapid adoption of computer-based testing paralleled this development. By the 1980s, the research literature was replete with considerations of the inherent advantages and limitations of automated assessment of a myriad of clinical domains. In particular, the application of computers to the evaluation of cognition has been widely studied. This body of research has generally fallen into one of two categories: (1) the translation of existing standardized tests to computerized administration and (2) the development of new computer tests and batteries for the assessment of cognitive function. Somewhere between these two categories are approaches that have adapted existing tests in a new way using computer administration. The Cambridge Neuro-psychological Test Automated Battery (CANTAB) is an example of a battery that has successfully combined standard cognitive test paradigms with novel formats.

The transition from paper-and-pencil- to computer-based assessment is not necessarily straightforward, and both methods of administration have distinct advantages and drawbacks. Included among the multiple benefits of computerized tests that have been cited are their ability to cover a wider range of abilities while minimizing floor and ceiling effects, potential for more standardized administration, multiple versions applicable to repeated testing, and precisely record accuracy and speed of response with a level of sensitivity not possible in standard administrations. Another potential advantage of computerized test batteries over traditional paper-and-pencil assessments is their flexibility in terms of immediate adjustment to performance levels. Many batteries have the capability of automatically altering test order, presentation rate, and level of difficulty in response to ongoing test performance. Such characteristics can be critical both in early detection and also in extending the range of a test to be useful across the full range of cognitive performance in a given patient population.

In comparison with traditional neuropsychological assessment instruments, computerized tests may also represent a potential cost savings not only with regard to materials and supplies but also in the time required of the test administrator. Moreover, the nature of the computerized instruments may allow administration by health-care clinicians other than neuropsychologists, allowing greater scheduling flexibility in the reduced need for administration by trained personnel.

In the initial excitement of this new application of technology, however, some basic aspects of test development may have been sacrificed. One of the more persistent criticisms of computerized test batteries has been the general lack of adequately established psychometric standards (Schlegel & Gilliland, 2007). Whether included

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in the test development phase or as post hoc analyses, basic indices of psychometric properties are essential to the widespread acceptance of new cognitive test batteries. Schlegel and Gilliland (2007) have outlined the necessary elements of quality assurance assessments for computer-based batteries. They caution against the acceptance of computerized adaptations of paper-and-pencil tests based purely on face validity. Others have also warned that equivalence across these media cannot be assumed (Buchanan, 2002; Butcher, Perry, & Atlis, 2000; Doniger et al., 2006). At a minimum, differences in communication of instructions, stimulus presentation, and response format may yield significant differences in test performance, particularly in an older population. Differences in computer experience as an intervening variable in performance cannot be ignored. Failure to demonstrate equivalence between the examinee's experience of computer versus traditional test administration, limited—and for the elderly in particular, perhaps unfamiliar—response modality, and poorly designed computer-person interface has been problematic in early iterations of this new methodology.

CANTAB

The CANTAB was developed initially by adapting animal paradigms for cognitive testing (Robbins et al., 1994; Sahakian & Owen, 1992). At the same time, careful analysis of the processes underlying each cognitive domain yielded means for independent assessment of these processes in a systematic and controlled fashion. For example, in an adaptation of the widely used Tower of London test of planning, the CANTAB Stockings of Cambridge tasks involve two stages. In the first, the subject works out and executes a series of steps to replicate a presented configuration; in the second, the subject must arrive at the correct response by mentally solving the series of moves without actually moving the stimuli. The multiple measures obtained during these tasks are then related to discrete cognitive functions that in turn are associated with activation of specific neural networks. The capability of a computerized test battery with a well-defined theoretical foundation to dissect performance on a test of executive function, for example, into multiple related but independent factors is a unique asset in furthering our knowledge of brain–behavior relationships.

In its original format first presented over 20 years ago (Sahakian, 1990), the CANTAB consisted of three batteries of tests designed to measure visual memory, attention, and planning. Over the years the battery has expanded to include tests designed to assess visual and verbal memory, executive function, attention, decision-making and response control, and social cognition. In addition two short "induction" tests can be used to familiarize participants with the general testing milieu and response format. The publishers of the CANTAB have also assembled "core batteries" for various diagnostic applications such as attention-deficit/hyperactivity disorder (ADHD), mild cognitive impairment (MCI), and schizophrenia, to provide focused assessments of the cognitive domains relevant to each disorder.

The nature of automated tests such as the CANTAB makes possible investigations of executive function across the life span. With minimal reliance on language, and continuous and immediate adjustment to level of performance, the CANTAB is well suited to help clarify age-related changes in specific executive abilities. DeLuca et al. (2003) selected CANTAB tests thought to tap working memory, strategic planning, organization of goal-directed behavior, and set-shifting in a study of a normative sample between the ages of 8 and 64. After administration of the Spatial Span (SSP), Spatial Working Memory (SWM), Tower of London, and Intra-/Extra-Dimensional Set-Shifting (IED) tests to 93 males and 101 females, the authors concluded that the CANTAB was sensitive to age and gender effects on executive function.

Another important parameter of test batteries purported to be well suited to repeat administration, and tracking of change over time or with intervention, is test-retest reliability. Lowe and Rabbitt (1998) administered all tests of the

CANTAB on two occasions separated by 4 weeks. The authors hypothesized that practice effects may be a more significant issue for tests that assess frontal or executive functions than tests of temporal function, as the former tend to rely on identification of strategies for successful performance. Further, as task novelty decreases with repetition, practice effects and individual variability in improvement with repeat testing may be amplified. Participants, ages 60–80, were selected to represent a range of ability as measured by a test of fluid intelligence. Practice effects were found to vary with test, task difficulty, level of intellectual ability, and outcome parameters. In general, test-retest correlations were higher for tests of memory than for tests of planning or working memory. More specifically, measures such as number of moves to solution on the Tower of London had poor test-retest correlations. On some tests higher intelligence was related to greater improvement with practice, while on others the opposite was true. Speed versus accuracy measures also differed in their sensitivity to repeat testing. The authors recommend the use of correction factors for practice effects where available, or at a minimum, obtaining good baseline data by allowing participants' practice trials dependent on the task.

The CANTAB has been used extensively in research settings as well as in clinical trials and has a published bibliography of over 700 articles assessing over 100 disorders. For the purposes of this review, discussion will be limited to those publications addressing deficits in executive function. Further, we focus on a selection of diagnostic groups that represent some of the main targets of research with this instrument. Thus, the bulk of the discussion will review studies of ADHDs and autism spectrum disorders (ASD) in childhood, followed by an overview of work in age-related cognitive decline, disorders of the frontal lobe, and finally Huntington's disease as an exemplar of a progressive neurodegenerative disorder with executive function implications. While it is beyond the scope of this chapter to summarize all relevant research efforts even in these diagnostic categories, every effort has been made to include those articles describing the most rigorous scientific methodology.

CANTAB Tests

The CANTAB can be administered by a trained assistant without reliance on verbal instruction. Responses are by touch screen or with a response button, depending on the task demands. Each task begins with practice items at a basic level. The design and interface of the CANTAB tests thus attempt to minimize effects of computer experience and computer-related anxiety. The tests described below are those that assess executive function and related domains; additional tests of verbal and visual memory and social cognition that are part of the complete battery are beyond the scope of this chapter but are described on their website (http://www.cambridgecognition.com).

Attention Switching Task (Goldberg et al., 2005). The participant is initially instructed to press a left or right button in response to the direction in which an arrow in the center of the screen is pointing. The second phase requires the participant to attend to a cue at the top of the screen that will determine whether the response reflects the direction in which the arrow is pointing or the side of the screen on which the arrow is located. Outcome measures include speed, accuracy, and types of errors (commission and omission), as well as switch cost and congruency cost.

Intra-/Extra-Dimensional Set Shift (*IED*). This test, described as a computer-based analog of the Wisconsin Card Sorting Test, assesses set formation and maintenance, shifting, and attentional flexibility. The task includes nine stages of increasing difficulty. The test initially presents two simple colored shapes and the participant must determine which one is correct in response to feedback. In successive stages when criterion is reached (i.e., six correct responses), the rules and/or stimuli change, moving from intra-dimensional, in which colored shapes remain the only relevant dimension, to extra-dimensional,

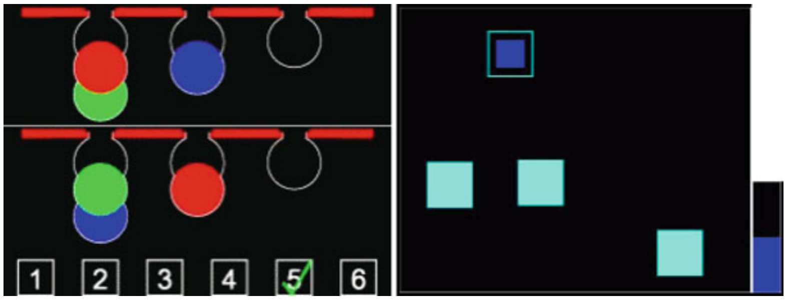

Fig. 11.1 One-Touch Stockings of Cambridge (*left*) and Spatial Working Memory (*right*) tasks

in which the participant needs to shift between white lines and colored shapes as relevant or irrelevant dimensions. Among the multiple outcome measures are errors to criterion, number of trials and stages completed, and response latencies.

Stockings of Cambridge (*SOC*). Based on the Tower of London test, the SOC is a measure of spatial planning in which the participant attempts to move colored balls to match a displayed pattern in the least possible number of moves. The time taken to complete the pattern, number of moves taken, and trials performed in minimum number of moves are measured.

One-Touch Stockings of Cambridge (*OTS*). This test relies on working memory in addition to spatial planning. In this task, two arrays of colored balls are presented. The participant's task is to choose from a series of numbered boxes, the minimum number of moves required to achieve the upper display by rearranging the lower array. The response is based on working out the solution without actually moving any balls. Outcome measures are based on speed and accuracy of response and include problems solved on first choice, mean choices to correct response, latency to first choice, and latency to correct choice.

Spatial Span (*SSP*). Described as a visual analog of the Digit Span Test, in this task white squares in an irregular array change color briefly in random sequences. The participant touches the boxes in the same order, or in reverse order, for varying sequence spans. The initial span consists of two boxes changing color up to a maximum of nine. The test is discontinued after three consecutive errors at a given span. Span length, errors, number of attempts, and latency are recorded.

Spatial Working Memory (*SWM*). Participants are asked to search through randomly arrayed boxes to locate colored tokens within the boxes, in order to fill a column on the side of the display. The number of boxes is increased over trials to a maximum of eight boxes. Measures of latency, errors, and a measure of search strategy are among the main outcome measures for this task. Errors can be further analyzed as "between-search" errors in which the subject returns to a box which has already been found to contain a token and "within-search" errors in which a box already opened and found to be empty earlier in the same trial is touched (Fig. 11.1).

Rapid Visual Information Processing (*RVP*). In this test of sustained attention, a white box appears in the center of the screen, containing single digits that appear in random order. The participant's task is to monitor the sequence of digits to match a target three-digit sequence. Measures of latency, hits and misses, false alarms, and rejections are tabulated.

Cambridge Gambling Task (*CGT*). Used to assess decision-making and risk-taking behavior, this task asks the participant to guess whether a yellow token is hidden in a red box or a blue box of ten boxes displayed across the screen. The proportion of red to blue boxes varies, as does the percent of "points" the participant chooses to gamble on the correctness of their choice. The test aims to separate out risk-taking from impulsivity, as the point percents are presented in ascending or descending order, forcing the participant to wait to make a high-risk bet. Outcome measures can include quality of decision-making (i.e., whether the subject chose the more likely outcome), time taken to choose, "bet" size, and risk adjustment.

Stop Signal Task (*SST*). This is a response inhibition test of two parts. In the first, participants are instructed to press a left- or right-hand button in response to an arrow pointing in that direction. In the second set of trials arrows continue to appear but the response is to be withheld if an auditory signal precedes the arrow presentation. Outcome measures include direction errors, proportion of successful stops, go-trial reaction time, stop-trial errors, and stop signal reaction time.

Assessing Executive Functioning in Childhood

Until recently, little research had been conducted on executive functioning in childhood, as it was believed that these cognitive skills did not develop until adolescence (DeLuca et al., 2003; Golden, 1981; Hughes & Graham, 2002). This paucity of research on executive functioning in children has been tied to three major factors (DeLuca et al., 2003). First, it was thought that the prefrontal cortex only became functionally mature late in development (i.e., late in adolescence or early adulthood) (Golden, 1981; Stuss, 1992). Second, several primate studies and early research on traumatic brain injuries suggested that juvenile prefrontal lesions had little or no consequence until later in adulthood (Walker, Husain, Hodgson, Harrison, & Kennard, 1998). Third, as standardized measures of executive functioning were designed to be difficult, these measures were often inappropriate for use with children, leaving this group of individuals without formal assessments of these domains of cognitive functioning (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Hughes & Graham, 2002; Kempton et al., 1999).

However, more recent investigations into executive functioning in children have suggested that these processes develop much earlier than once thought, beginning around 12 months of age, with a burst in development around 8 years of age (Ardila & Roselli, 1994; Case, 1992; DeLuca et al., 2003; Luciana & Nelson, 1998). Additionally, these early increases in executive functioning have been correlated with increased myelination and synaptogenesis in the frontal regions during these periods of growth (DeLuca et al., 2003; Espy, 1997; Kempton et al., 1999; Klingberg, 1997). Furthermore, life-span studies of executive functioning show that a number of domains, including short-term memory and sequencing, working memory, strategic planning and organization, and attentional set-shifting, appear to be present and measurable between ages 8 and 10 years, with the greatest functional gains in performance in each of these domains appearing between 15 and 30 years of age, followed by a gradual decline in performance over time with aging (DeLuca et al., 2003). Thus, there is much evidence to support the development executive functioning in children, and as such, there is an increased need to develop standardized executive functioning assessment measures that are appropriate for use with children.

The increased interest in the childhood development of executive functioning has been sparked by the study of clinical populations, as well as the development of several new assessment methods, which have been shown to be appropriate for use with children (Hughes & Graham, 2002). Of particular interest, several neurodevelopmental disorders have been shown to be associated with specific impairments in executive functioning, with the greatest body of literature providing evidence for these deficits in ADHD and ASD (Hughes & Graham, 2002; Ozonoff, 1997). Specifically, children with ADHD have been shown to have deficits primarily in inhibitory control, which is likely rooted in frontostriatal circuitry and decreased volume in dorsolateral prefrontal cortex, caudate, and cerebellum, as well as difficulty with strategic flexibility, planning, working memory, monitoring, and sustained attention (Chamberlain et al., 2011). In contrast, executive functioning deficits in ASD have been more often characterized by high-level cognitive, nonspatial problems, such as deficits in planning and set-shifting, as well as more secondary deficits in working memory (Hill, 2006). Furthermore, numerous studies of preschoolers have demonstrated that individual differences in executive functioning are correlated with individual differences in theory of mind, or the ability to attribute mental states to the self and others, which is a well-established deficit among individuals with ASD (Hughes & Graham, 2002; Perner & Lang, 1999).

In addition to the growth of research in the domain of executive functioning deficits in neurodevelopmental disorders, the study of normative development of executive functioning in childhood has also received increased attention. This increased focus has resulted in the development of numerous executive functioning assessment measures, which propose to be appropriate for broad age groups (Hughes & Graham, 2002; Hughes, Plumet, & Leboyer, 1998; Manly et al., 2001). However, children differ from adults in a number of important ways, and to fully assess executive functioning in children, executive functioning assessment measures must make accommodations for these differences. Specifically, children have limited language abilities and tend to have poorer motivation than adults; thus, child-appropriate measures of executive functioning need to be easy to understand, relatively independent of language skills, somewhat simplified, and in order to maintain motivation, somewhat fun (DeLuca et al., 2003; Hughes & Graham, 2002). Furthermore, in order to assess the development of executive functioning over time in both typically developing and neurodevelopmentally delayed populations, executive functioning assessment tools must be standardized across broad age ranges and populations, allowing for more reliable and valid longitudinal assessments (Hughes & Graham, 2002).

Computerized testing batteries of executive functioning may help to address several of the issues associated with the assessment of executive functioning both in children and across development. Specifically, these testing batteries can tap into a wide range of abilities, reduce floor and ceiling effects, reduce human error with more standardized formats, more precisely record speed and accuracy, reduce reliance on verbal instructions and feedback, and increase the potential for widespread screening efforts across broad age ranges (DeLuca et al., 2003; Wild, Howieson, Webbe, Seelye, & Kaye, 2008). In particular, the CANTAB may be uniquely suited to the assessment of executive functioning in children (Chamberlain et al., 2011; DeLuca et al., 2003). The CANTAB has the benefit of being widely used in academic studies with children from age 4 years and upwards (Chamberlain et al., 2011), with standardized scores and age-normative data available for individuals aged 8–80 years (Chamberlain et al., 2011; DeLuca et al., 2003; Hughes & Graham, 2002). Furthermore, the CANTAB has been shown to be sensitive to impairments in school-aged children with ADHD, ASD, and other neurodevelopmental disorders (Chamberlain et al., 2011; Hughes & Graham, 2002). In fact, recent reviews suggest that over 30 studies have utilized the CANTAB to examine executive functioning deficits in individuals with ADHD, and 20 studies have done so in individuals with ASD. We now turn our attention to a review of these literatures beginning with ADHD.

Evaluating Executive Functioning Using CANTAB in ADHD

According to DSM-IV criteria, ADHD includes the symptom domains of inattention/distraction and hyperactivity/impulsivity (American Psychological Association, 2000). Impairments in executive functioning are suggested both by the core diagnostic criteria of ADHD, with dysregulation of attention, behavior, and impulse control at the heart of the disorder, and disruptions to the frontostriatal circuitry, as supported by neuroimaging studies, which have revealed reduced volumes in the dorsolateral prefrontal cortex, caudate, and cerebellum (Seidman, Biederman, Monuteaux, & Doyle, 2005; Valera, Faraone, Murray, & Seidman, 2007). Specifically, children with ADHD have been shown to have deficits in primarily inhibitory control, as well as difficulty with strategic flexibility, planning, working memory, self-monitoring, and sustained attention (Chamberlain et al., 2011).

The CANTAB has been widely used in the study of executive functioning deficits associated with ADHD, as well as in the study of the effects of pharmaceutical treatment on both improving executive functioning and reducing symptoms among individuals with ADHD. In fact, in a recent meta-analysis by Chamberlain et al. (2011), 13 studies examining performance on CANTAB subtests compared participants with ADHD and typically developing controls. According to this meta-analysis, medium to large effects were observed in participants with ADHD when compared to typically developing controls on the CANTAB sub-domains of response inhibition, working memory, and executive planning, with smaller effects observed in attentional set-shifting (Chamberlain et al., 2011). An additional review of the literature on the effects of salient drugs on executive functioning, as assessed by the CANTAB, in individuals with ADHD revealed that methylphenidate (Ritalin) improved working memory, modafinil improved planning, and methylphenidate, modafinil, and atomoxetine all improved inhibition (Chamberlain et al., 2011). We now turn our attention to a more in-depth examination of these literatures beginning with an examination of the literature on inhibition as assessed by the CANTAB in individuals with ADHD.

Inhibition as Assessed by the CANTAB in ADHD. Inhibition is assessed with the CANTAB using the SST, which is a classic stop signal response inhibition test. As described above, the meta-analysis by Chamberlain et al. (2011) found a large deficit in stop signal reaction time when individuals with ADHD were compared to typically developing individuals across four studies. Specifically, individuals with ADHD were found to have longer stop signal reaction times; however, individuals with ADHD did not differ from controls with respect to their reaction times on go trials, suggesting that the deficit is specific to inhibition. These findings are similar to those that have been reported in other meta-analyses using other computerized SSTs, as well as other measures of inhibition, such as the Stroop task (Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005; Lijffijt, Kenemans, Leon, Verbaten, & van Engeland, 2005; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Additionally, this deficit has been observed in both children (Brophy, Taylor, & Hughes, 2002; DeVito et al., 2008; Goldberg et al., 2005; Rhodes, Coghill, & Matthews, 2005) and adults (Aron, Dowson, Sahakian, & Robbins, 2003; Chamberlain et al., 2007; Clark et al., 2007; McLean et al., 2004; Turner, Clark, Dowson, Robbins, & Sahakian, 2004). Thus, the deficit in inhibition appears to be rather robust among individuals with ADHD (Garcia-Villamisar & Hughes, 2007).

These deficits have been associated with disrupted neural networks, including right inferior frontal gyrus, bilateral anterior cingulate cortex, and the superior motor region (Clark et al., 2007; Goldberg et al., 2005). Additionally, inhibition is thought to be under the control of catecholamines, specifically dopamine and norepinephrine, as several studies have shown that medications which alter dopaminergic and noradrenergic functioning improve inhibition and stop signal reaction times among individuals with ADHD (Aron et al., 2003; Chamberlain et al., 2007; DeVito et al., 2008; Turner et al., 2004). Specifically, in an acute, double-blind, placebo-controlled crossover study, Aron et al. (2003) found that methylphenidate ameliorated the deficit in stop signal reaction time among adults with ADHD, and DeVito et al. (2008) replicated these results in children. Additionally, Coghill, Rhodes, and Matthews (2007) found that chronic treatment of ADHD with methylphenidate improved performance on the SST among children. In contrast, Rhodes, Coghill, and Matthews (2006) did not observe the amelioration of the slowed stop signal reaction time among children with ADHD in a randomized, double-blind, placebo-controlled study with methylphenidate; however, it should be noted that this study utilized a low-dose design. Thus, it may be that dosing and duration of treatment with methylphenidate play a role in the treatment of disinhibition among individuals with ADHD.

It should also be noted that similar results were observed in acute, double-blind, placebo-controlled crossover studies with atomoxetine in children (Gau & Shang, 2010b) and adults with ADHD (Chamberlain et al., 2007), and modafinil has been shown to have similar effects in adults with ADHD (Turner et al., 2004). Therefore, the treatment effects do not appear to be specific to a particular medication; however, these effects do appear to be limited to those medications that target both norepinephrine and dopamine.

Interestingly, the results observed among individuals with ADHD were also shown to be relevant to healthy controls. In two acute, double-blind, placebo-controlled studies with atomoxetine, one parallel and one crossover design, significant increases in stop signal reaction times were observed among healthy adult volunteers (Chamberlain et al., 2006, 2009). In an fMRI study, the use of atomoxetine was found to increase right, frontal inferior cortex activation during the CANTAB stop signal task among healthy adult volunteers (Chamberlain et al., 2009). However, mixed results have been observed in similar trials using both methylphenidate and modafinil with some studies finding increases in stop signal reaction time and some studies finding no treatment effects (Turner et al., 2003, 2004; Winder-Rhodes et al., 2009). Finally, in a single acute, double-blind, placebo-controlled, parallel study with guanfacine in healthy adult volunteers, an overall global slowing of reaction time on both go and stop trials was observed, suggesting that guanfacine may act as a sedative, resulting in increased inhibition (Muller et al., 2005).

Working Memory as Assessed by the CANTAB in ADHD. In addition to deficits in inhibition, deficits in working memory among individuals with ADHD have also been reported in a meta-analysis of ten studies with a large effect size (Chamberlain et al., 2011). In particular, working memory on the CANTAB is assessed with the SWM Task, which assesses an individual's ability to retain spatial information and manipulate remembered items in working memory. Meta-analytic results suggest that the greatest impairments are in the areas of between-search errors and strategy, with individuals with ADHD having more errors and worse strategy scores than typically developing controls. Furthermore, this is consistent with previous meta-analytic work examining other SWM tasks revealing SWM deficits in ADHD (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Willcutt et al., 2005). As with the observed effect on inhibition, the working memory deficit associated with ADHD has also been observed in both children (Barnett et al., 2001; Gau, Chiu, Shang, Cheng, & Soong, 2009; Gau & Shang, 2010a; Goldberg et al., 2005; Kempton et al., 1999; Klingberg, Forssberg, & Westerberg, 2002; Rhodes, Coghill, & Matthews, 2004; Vance, Maruff, & Barnett, 2003) and adults (Chamberlain et al., 2007; Clark et al., 2007; Dowson et al., 2004; Gropper & Tannock, 2009; McLean et al., 2004). The SWM deficit may serve as an endophenotype of ADHD, as typically developing siblings of children with ADHD have also been shown to display deficits on this measure (Gau & Shang, 2010a). Additionally, poor performance on SWM in individuals with ADHD has also been linked to poor academic achievement among young adults and poor performance on progressive matrices tasks, increased motor activity, and poor inhibition among children (Clark et al., 2007; Gropper & Tannock, 2009; Klingberg et al., 2002).

Again, the catecholamines, dopamine and norepinephrine, have been implicated in the deficits in working memory observed among individuals with ADHD, as the medications which have been found to improve SWM in both children and adults with ADHD have all been shown to target the production or to block the reuptake of these neurotransmitters. Specifically, methylphenidate has been shown to improve performance on the CANTAB spatial working memory test in both children (Barnett et al., 2001; Bedard, Martinussen, Ickowicz, & Tannock, 2004; Brophy et al., 2002; Hoare & Sevar, 2007; Kempton et al., 1999; Mehta, Goodyear, & Sahakian, 2004) and adults (Turner, Blackwell, Dowson, McLean, & Sahakian, 2005). In contrast, two studies found no effects of methylphenidate on SWM among children, though both of these were low-dose trials (Coghill et al., 2007; Rhodes et al., 2004). Methylphenidate was also observed to increase accuracy on the SWM task in healthy adults, with PET imaging results suggesting that improved performance was associated with increased binding of dopamine in the striatum (Mehta, Calloway, & Sahakian, 2000).

The effect of medications other than methylphenidate on SWM performance in individuals with ADHD is less conclusive with studies reporting mixed results. In particular, atomoxetine has been shown to improve spatial short-term memory among children in an acute, double-blind, placebo-controlled study (Gau & Shang, 2010b), but no effects were observed in a similar trial with adults (Chamberlain et al., 2011). Similarly, modafinil improved short-term spatial memory span in one acute, double-blind, placebo-controlled trial (Turner et al., 2004), but not another (Turner et al., 2005). Finally, in an acute, double-blind, placebo-controlled crossover study with healthy volunteers, guanfacine improved accuracy, but not strategy scores on the CANTAB spatial working memory task, though no studies of the effects of this medication on SWM among patients with ADHD were found (Jakala et al., 1999).

Executive Planning as Assessed by the CANTAB in ADHD. Another major deficit observed among individuals with ADHD is in domain of executive planning. With respect to the CANTAB, executive planning is assessed with the Stockings of Cambridge subtest. In a meta-analysis of six studies using the CANTAB Stockings of Cambridge task in ADHD, individuals with the disorder were showed to have deficits falling in the medium effect size range on this executive planning task (Chamberlain et al., 2011), which is similar to the effects sizes reported in previous meta-analyses of executive planning deficits in ADHD (Willcutt et al., 2005). The majority of research examining executive planning deficits associated with ADHD using the Stockings of Cambridge subtest has been conducted with children (Brophy et al., 2002; Gau et al., 2009; Gau & Shang, 2010a; Kempton et al., 1999; Rhodes et al., 2005) with all but one study showing significant deficits in accuracy among children with ADHD (Goldberg et al., 2005). However, a single study of executive planning in adults with ADHD, using the Stockings of Cambridge subtest, found significant deficits in executive planning among adults with ADHD when compared to typically developing adults (McLean et al., 2004).

Among individuals with ADHD, performance on the Stockings of Cambridge test appears to be relatively unaffected by medication with the majority of studies being conducted with methylphenidate (Bedard et al., 2004; Coghill et al., 2007; Mehta et al., 2004; Rhodes et al., 2006). However, a single acute, double-blind, placebo-controlled crossover study of adults did report increased accuracy on the Stockings of Cambridge test following treatment with 200 mg of modafinil (Turner et al., 2004). Medication also appears to have an effect on accuracy on this task among healthy adults. Specifically, guanfacine and modafinil have both been shown to enhance performance accuracy and planning on the Stockings of Cambridge in healthy adults in acute, double-blind, placebo-controlled crossover and parallel designed studies (Jakala et al., 1999; Muller et al., 2005; Turner et al., 2003; Winder-Rhodes et al., 2009).

Attentional Set-Shifting as Assessed by the CANTAB in ADHD. The CANTAB assesses attentional set-shifting using the IED task. According to a recent meta-analysis of eight studies, individuals with ADHD perform significantly worse on the IED task than typically developing controls with respect to overall number of errors (Chamberlain et al., 2011). This was a somewhat smaller effect than others that have been reported previously, with deficits in attentional set-shifting in the medium effect size range for individuals with ADHD when compared to typically developing controls on the Wisconsin Card Sorting Task (Willcutt et al., 2005).

Five studies comparing children with ADHD with typically developing controls reported reduced accuracy and stages completed among the ADHD group with the greatest differences observed in the final stages of the task, particularly the extra-dimensional shifting stages (Gau et al., 2009; Gau & Shang, 2010a; Kempton et al., 1999; Rhodes et al., 2005; Vance et al., 2003). Additionally, Brophy et al. (2002) reported that while hard-to-manage children showed intact set-shifting, compared to typically developing children, they made more perseverative and rule-based errors, suggesting that they performed qualitatively differently from typically developing youth. In contrast, one study reported no such difference among children with and without ADHD (Goldberg et al., 2005). Similarly, two such studies have been conducted with adults with one reporting significant differences between ADHD and controls on accuracy during the extra-dimensional shifting stage (McLean et al., 2004) and one reporting no such differences (Chamberlain et al., 2007). It should also be noted that healthy, unaffected siblings of children with ADHD also display impaired set-shifting abilities, making more extra-dimensional shift errors, suggesting that there may be a genetic component to this specific measure of executive functioning (Gau & Shang, 2010a). Thus, it may be that while overall set-shifting ability remains somewhat intact among individuals with ADHD, there may be both qualitative and quantitative differences in performance on this task at greater levels of difficulty, and these differences may serve as an endophenotype of ADHD.

This set-shifting deficit observed among individuals with ADHD also appears to be relatively unaltered by salient mediations. Only one acute, placebo-controlled parallel study of children with ADHD treated with methylphenidate reported improved accuracy and stages completed following treatment (Mehta et al., 2004), while several others reported no such effect using similar study designs using both children and adults treated with atomoxetine, methylphenidate, and modafinil (Chamberlain et al., 2007; Coghill et al., 2007; Rhodes et al., 2006; Turner et al., 2005). Additionally, no studies have reported significant improvements among healthy volunteers treated with atomoxetine, guanfacine, methylphenidate, or modafinil in any of the nine published placebo-controlled studies reviewed (Elliot et al., 1997; Garcia-Villamisar & Hughes, 2007; Jakala et al., 1999; Muller et al., 2005; Randall et al., 2005; Randall, Fleck, Shneerson, & File, 2004; Randall, Shneerson, Plaha, & File, 2003; Rogers, 1999; Turner et al., 2003, 2004), and in fact, both methylphenidate and modafinil have been shown to impair extra-dimensional set-shifting in healthy adult volunteers (Randall et al., 2004; Rogers, 1999). As such, it may be that this domain of executive functioning is under control of a unique system of neurotransmitter control other than the noradrenergic or dopaminergic systems that these drugs typically target.

Other Domains of Cognitive Functioning Assessed by the CANTAB in ADHD. In addition to those aspects of executive functioning assessed by the CANTAB described above, assessments of sustained attention/vigilance are also relevant. In particular, the CANTAB rapid visual information processing test assesses sustained attention and vigilance, which is similar to several other continuous performance tasks. Two studies found that individuals with ADHD were less accurate at identifying targets (more commission errors) than typically developing controls (Bedard et al., 2004; Turner et al., 2004). Furthermore, it was also reported that both methylphenidate and modafinil reduced these errors in individuals with ADHD, while atomoxetine did not (Bedard et al., 2004; Chamberlain et al., 2006; Turner et al., 2004). Additionally, modafinil has been shown to enhance performance, by increasing accuracy of identifying targets, among healthy adult volunteers (Randall et al., 2005).

Summary of Executive Functioning Assessed by the CANTAB in ADHD. When assessed with the CANTAB, children with ADHD have been shown to have deficits in inhibitory control and working memory, as well as more secondary deficits in executive planning, strategic flexibility/attentional set-shifting, and sustained attention (Chamberlain et al., 2011). Additionally, these findings are congruent with neuroimaging studies which have reported disruptions to the frontostriatal circuitry and specifically reduced volumes in the dorsolateral prefrontal cortex, caudate, and cerebellum (Seidman et al., 2005; Valera et al., 2007). Finally, it has been shown that specific salient drugs have an ameliorating effect on executive functioning deficits in ADHD as assessed by the CANTAB. Specifically, methylphenidate (Ritalin) has been demonstrated to improve working memory, modafinil improves planning, and methylphenidate, modafinil, and atomoxetine all improve performance on tests of inhibition (Chamberlain et al., 2011).

Evaluating Executive Functioning Using CANTAB in Autism Spectrum Disorders

Turning our attention to autism and autism spectrum disorders, these are a class of neurodevelopmental disorders characterized by impaired social interaction and communication, as well as restricted interests and repetitive behaviors (American Psychological Association, 2000). The autism spectrum disorders include autism, Asperger's syndrome, which lacks the delays in cognitive development and language often observed in autism, and pervasive developmental disorder-not otherwise specified (American Psychological Association, 2000). Overt symptoms of these disorders gradually begin around age 6 months and become well established by age 2 or 3 years (American Psychological Association, 2000). Autism is associated with significant impairment and present in less than 1 % of all youths with a 4:1 male-to-female ratio. However, the prevalence of Asperger's syndrome is somewhat debated, as it is difficult to distinguish from high-functioning autism, though it is also believed to be less than 1 % of all youths with a male-to-female ratio ranging from 1.6:1 to 4:1 (Mattila et al., 2007).

Executive functioning deficits in these disorders have been more often characterized by high-level cognitive, nonspatial problems, such as deficits planning and set-shifting, as well as secondary deficits in inhibition and working memory. Additionally, milder versions of these deficits have also been observed among first-degree, healthy relatives of individuals with ASDs, and these deficits have been linked to several ASD-specific behaviors, including perseverative focus on details and the display of highly specific interests. Furthermore, numerous studies of preschoolers have demonstrated that individual differences in executive functioning are correlated with individual differences in theory of mind, or the ability to attribute mental states to the self and others, which is a well-established deficit in individuals with ASD (Hughes & Graham, 2002; Perner & Lang, 1999). Taken together, these findings suggest that executive dysfunction in these domains may serve as an endophenotype of ASD. We now turn our attention to specific domains of executive functioning which have been assessed using CANTAB in individuals with autism and autism spectrum disorders.

Executive Planning as Assessed by the CANTAB in ASD. Executive planning refers to a complex, dynamic sequence of planned actions that must be constantly monitored, reviewed, and updated. The CANTAB assesses executive planning with the Stockings of Cambridge test. Individuals with autism tend to perform worse than control groups on this task, including groups composed of individuals with ADHD, Tourette's syndrome, cognitive age-matched individuals with other developmental disabilities, and typically developing controls (Happe, Booth, Charlton, & Hughes, 2005; Hill, 2006; Hughes, Russell, & Robbins, 1994; Ozonoff et al., 2004; Sinzig, Morsch, Bruning, Schmidt, & Lehmkuhl, 2008; Witwer & Lecavalier, 2008), suggesting that there may be unique deficits in executive planning associated with autism spectrum disorders that are not present in other forms of neurodevelopmental disorders or psychopathology (Ozonoff et al., 2004; Sinzig et al., 2008). Furthermore, this impairment has been shown to be present in children and adolescents with autism and to be sustained over time in both cross-sectional and longitudinal studies of individuals with autism (Bramham et al., 2009; Garcia-Villamisar & Hughes, 2007). Additionally, impaired performance on the Stockings of Cambridge task has been observed among first-degree relatives of individuals with autism spectrum disorders, suggesting that deficits in executive planning may serve as an endophenotype of the disorder (Hughes & Graham, 2002; Hughes, Plumet, & Leboyer, 1999).

Attentional Set-Shifting as Assessed by the CANTAB in ASD. The CANTAB assesses attentional set-shifting using the IED task. In general, individuals with autism spectrum disorders tend to show deficits in attentional set-shifting and cognitive flexibility, as illustrated by difficulties they have with perseverative and stereotyped behaviors and interests (Hill, 2006), and individuals with autism spectrum disorders tend to respond to the IED and other tasks like it, such as the Wisconsin Card Sorting Task, with perseverative responding especially when shifting to a new rule or demand (Geurts, Corbett, & Solomon, 2009; Hill, 2006; Landa & Goldberg, 2005; Ozonoff et al., 2004). This deficit in attentional set-shifting among individuals with autism spectrum disorders has been observed in both children (Geurts et al., 2009; Landa & Goldberg, 2005; Ozonoff et al., 2004) and adults (Berger, Aerts, van Spaendonck, Cools, & Teunisse, 2003). The deficit has also been observed when individuals with ASD are compared to individuals with other neurodevelopmental disorders and typically developing controls (Hughes et al., 1994) and when matched according to age, the presence or absence of a learning disorder (Hughes et al., 1994), and/or verbal and nonverbal developmental age (Sinzig et al., 2008; Teunisse, Cools, van Spaendonck, Aerts, & Berger, 2001). As with executive planning, deficits in attentional set-shifting have also been observed as assessed on the Stockings of Cambridge task among healthy parents and siblings of individuals with autism spectrum disorders (Hughes et al., 1999; Hughes & Graham, 2002).

Inhibition as Assessed by the CANTAB in ASD. While there is a great deal of evidence to support deficits in inhibition among individuals with ADHD as assessed by the CANTAB using the SST (Chamberlain et al., 2011), as well as a number of other assessments of inhibition (Boonstra et al., 2005; Lijffijt et al., 2005; Willcutt et al., 2005), the picture is somewhat less clear in individuals with autism spectrum disorders. Specifically, inhibition (i.e., stop signal reaction time) on the SST has been shown to be relatively intact among children with autism spectrum disorders when compared both to children with ADHD and typically developing children (Corbett, Constantine, Hendren, Rocke, & Ozonoff, 2009; Edgin & Pennington, 2005; Geurts et al., 2009). However, children with autism spectrum disorders have been shown to display impaired vigilance and faster overall reaction times (i.e., both on go and stop trials) than typically developing children (Corbett et al., 2009; Edgin & Pennington, 2005). Finally, qualitative data suggest that children with autism spectrum disorders tend to view the rules of this task as somewhat arbitrary and have been reported to develop maladaptive strategies when self-reported understanding of the goals of this task has been assessed (Hill, 2006).

Working Memory as Assessed by the CANTAB in ASD. As with inhibition, there is evidence that the primary deficits observed in tasks of working memory as assessed by the CANTAB may be due to the use of maladaptive strategies or poor understanding of the rules (Steele, Minshew, Luna, & Sweeney, 2007). However, there is evidence of individual differences and heterogeneity in working memory skills both among individuals with autism spectrum disorder and their first-degree relatives (Garcia-Villamisar & Hughes, 2007). For example, healthy siblings of individuals with autism spectrum disorders have been shown to have superior SSPs, but there were no observed differences when compared to typically developing individuals with respect to working memory performance per se (Hughes et al., 1999). Others have shown improved visuospatial functioning among all autism spectrum disorder probands (Lajiness & Menard, 2008).

Summary of Executive Functioning Assessed by the CANTAB in ASD. Autism and autism spectrum disorders have been characterized by high-level cognitive, nonspatial problems, such as deficits in planning and set-shifting, as well as secondary deficits in inhibition and working memory. These findings are congruent with neuroimaging studies that have reported both structural abnormalities in the prefrontal cortexes of individuals with autism and reduced dorsolateral and ventromedial prefrontal cortex activity during these tasks among individuals with autism when compared to typically developing controls (Berger et al., 2003; Hill, 2006; Ozonoff et al., 2004). Additionally, milder versions of these deficits have been observed among first-degree, healthy relatives of individuals with ASDs, suggesting that executive dysfunction in these domains may serve as an endophenotype of ASD. Finally, it should be noted that additional research into the roles of executive functioning in distinguishing specific subtypes of autism spectrum disorders is needed.

Assessing Executive Functioning in Older Adults

Despite its application to assessment of cognitive function in patients with disorders ranging from neurologic and psychiatric to metabolic and cardiac, the CANTAB was originally developed for use with older adults and those with dementia (Robbins et al., 1994). Robbins et al. (1994) administered the CANTAB as it existed in 1994 to a large sample of healthy older participants between the ages of 55 and 80, to begin to describe the effects of age, gender, and intelligence on performance. Scores on those subtests were found to successfully differentiate between different age groups and levels of intellectual ability. Eleven performance variables (e.g., accuracy and latency scores, learning trials, and error scores) were included in a factor analysis, yielding four factors interpreted as representing general learning and memory, speed of responding, executive processes, and visual perceptual ability. The factor structure was found to remain consistent across age groups and IQ test scores, but with differential loadings across the four factors based on IQ test scores.

In a later study focused on CANTAB tests of executive function, Robbins et al. (1998) reported results from a sample of healthy older adults. Three hundred forty-one participants were administered the Spatial Working Memory, Stockings of Cambridge, and Intra/Extra Dimensional Set Shift tests as well as CANTAB tests known to demonstrate age-related decline (i.e., tests of visual memory and learning). Greatest age-related declines were seen in attentional set-shifting, where the oldest age group (75–79) made significantly more errors than the rest of the group on extra-dimensional set shifts. On the Stockings of Cambridge planning task, older adults solved fewer problems in the minimum possible steps and had significantly longer response latencies than the youngest groups. The authors conclude that their findings are consistent with neuroimaging findings that have demonstrated age-associated changes in prefrontal cortex and striatum in addition to regions of the temporal lobes.

In an attempt to replicate these findings, Rabbitt and Lowe (2000) administered the CANTAB to 162 healthy older adults between the ages of 60 and 80 years. Unlike the earlier study, they found that tests of the CANTAB that are established measures of temporal lobe function (e.g., paired associates learning) were more age-sensitive than the frontal tasks. For example, scores on the IED and Stockings of Cambridge tests did not correlate with age, while in a linear regression analysis, age predicted performance on tests of visual memory. The authors conclude that the so-called frontal tests of the CANTAB are less sensitive to changes of normal aging than the tests that assess memory functions.

Disorders of Frontal Lobe Function and the CANTAB

In describing aspects of executive function that are sensitive to prefrontal cortical dysfunction, Robbins (1996) cites psychometric and neuroimaging evidence to demonstrate the ability of relevant CANTAB subtests to further characterize deficits in planning, working memory, and attentional set-shifting. For example, patients with frontal lobe deficits exhibit impaired performance with extra-dimensional set-shifting on the CANTAB Intra-/Extra-Dimensional Set Shift test. Specifically, the impairment has been attributed to a specific failure of response inhibition based on manipulation of test instructions to induce perseveration or learned irrelevance conditions, with frontal patients making more perseverative errors (Owen et al., 1993).

The two variations of the Tower of London test, i.e., Stockings of Cambridge and OTS, are thought to rely on different aspects of planning (actual motor sequencing vs. mental imagery). Functional neuroimaging studies in healthy controls have lent support for the different demands placed by these two versions of a planning task; while both activated dorsolateral prefrontal cortical areas, the "mental" task activations were greater on the right, while the "motor" format placed greater demands on the left frontal regions (Owen, Doyon, Petrides, & Evans, 1996). These findings have been posited to be a result of differential demands of the tasks on SWM and/or memory sequencing (Robbins, 1996).

In an earlier study of planning and working memory, 26 patients with frontal lobe excisions were compared with age-matched controls on a subset of CANTAB tests (Owen, Downes, Sahakian, Polkey, & Robbins, 1990). An average of 3 years following surgery, patients were found to make significantly more search errors both within and between trials and had less successful strategies on a test of SWM. On the Stockings of Cambridge planning task, they took more moves and solved fewer problems in the minimum possible moves than their healthy counterparts. Further, they were significantly slower to execute a response after a first move, raising the possibility of impulsivity in initiating response prior to constructing a successful solution. These same patients were unimpaired relative to the healthy controls on a test of short-term spatial memory. The authors identify "strategy deficits" as a key component of performance on both the working memory and planning tasks.

An examination of cognitive test performance of patients with mild frontotemporal dementia by Rahman, Sahakian, Hodges, Rogers, and Robbins (1999) further elucidates the heterogeneity of executive functions in the prefrontal cortex. Eight patients with FTD were compared with age-matched healthy controls on a range of tests of memory and executive function. They found that even in the relatively mild stages of the disease, impairments were revealed that might not be demonstrated by more traditional neuropsychological test batteries. Specifically, even in this small sample patients showed selective deficits as illustrated by performance on a decision-making task (CGT), in which they made poorer risk adjustments in response to changing odds of success. Further, there was some evidence of impairment, in attentional set-shifting, although the findings of Owen et al. (1990) with regard to increased errors at the extra-dimensional shift stage were not replicated. However, the FTD patients in this study did not differ from healthy controls in their performance on tests of pattern or spatial recognition memory, spatial span, working memory (SWM), or planning (OTS). The authors conclude that these findings are consistent with evidence from neuroimaging studies which suggests a progression of pathology in frontotemporal dementia from early orbitofrontal or ventromedial to more lateral prefrontal regions.

Evaluating Executive Functioning Using the CANTAB in Huntington's Disease

Since the discovery of the Huntington's disease mutation, accurate determination of the genetic status of at-risk individuals has made possible the study of cognitive function in preclinical HD patients. Further, tracking of cognitive decline from the earliest stages can be related to the known pattern of progression of neuropathology, from early involvement of the dorsal caudate nucleus to gradual deterioration throughout the frontostriatal system in a dorsal to ventral, anterior to posterior, and medial to lateral direction (Watkins et al., 2000). Tests of the CANTAB have been widely used to trace the progression of cognitive deficits in HD, adding to our understanding of the neural underpinnings of specific executive functions. Lawrence et al. (1998) compared HD mutation carriers with no movement disorders, with noncarriers on a battery of tests known to be sensitive to the early changes of the disease. As hypothesized, they found mutation carriers were more impaired in extra-dimensional shifting on a test of attentional set-shifting (IED), which they attribute to a deficit in inhibitory control as demonstrated by increased perseverative responses. Performance on tests of spatial span, spatial working memory, and spatial planning was no different between groups, suggesting a specific pattern of cognitive impairment in preclinical HD which is related to early basal ganglia dysfunction. The authors recommend the attentional set-shifting task as particularly sensitive to the earliest cognitive changes in HD, with implications for initiation of therapeutic interventions.

Watkins et al. have further delineated specific patterns of executive dysfunction in HD (Watkins et al., 2000). In a comparison of patients with mild HD versus age-matched healthy controls, patients had longer response latencies and made more errors on the One-Touch Stockings of Cambridge task, while on a decision-making test (CGT), they were slower to respond but were no different than controls on size of bet or impulsivity in response to changing risks and rewards. The findings that HD patients were impaired in planning but not in decision-making are in keeping with the known progression of pathology from early dorsal to later ventral caudate involvement. Previous work has shown the One-Touch Tower of London test to be sensitive to dorsolateral prefrontal cortical damage, while impaired decision-making has been associated with orbitofrontal cortical lesions (Watkins et al., 2000). The authors relate their findings to those of Rahman et al. (1999) with FTD patients to illustrate the dissociation between deficits in decision-making and planning in these patient groups, consistent with the involvement of dorsolateral PFC and relative preservation of orbitofrontal circuitry in early HD and the reverse in FTD.

In a similar effort to demonstrate qualitative differences in cognitive decline consistent with known neuropathology, patients with Huntington's disease and Alzheimer's disease were matched for level of dementia and compared on tests of visual memory and executive function (Lange, Sahakian, Quinn, & Robbins, 1995). Predictably, patients with HD had worse performance on tests of executive function including Spatial Working Memory, planning, and set-shifting. However they were also significantly more impaired relative to patients with AD on tests less clearly dependent on executive function, including tests of visual pattern recognition, spatial span, and visuospatial paired associates learning. While these patients with later-stage HD demonstrated fairly wide ranging cognitive impairment; the pattern of deficits was nevertheless qualitatively different from that of AD patients at a similar stage of disease progression.

In one of the few longitudinal studies of cognitive decline in HD, Ho et al. (2003) followed a sample of patients with mild to moderate disease for at least 3 years. While general cognitive ability remained unchanged, patterns of decline in executive function were identified, such that planning and set-shifting deteriorated over time. Specifically, measures of errors on the One-Touch Tower of London task and response latencies on the IED task were sensitive in detecting progression of cognitive impairment in this sample. Interestingly, similar decline in performance on the Wisconsin Card Sorting Test, a widely used test of executive function, was not found, leading the authors to suggest that the practice effects of learning a strategy make the WCST less useful in longitudinal assessment. Finally, they note that delineating the component features of executive processes relies on tests capable of finer gradations of measurement that are sensitive to change over time. Certainly, the growing body of evidence describing the progression of cognitive decline has been consistent with the known frontostriatal pathology of Huntington's disease.

Summary and Conclusions

The tests of the CANTAB have been used extensively to assess cognitive performance in a wide range of neurodegenerative and neurodevelopmental, psychiatric, and metabolic disorders, among others. The CANTAB has been shown to be useful in identifying and evaluating discrete components of important cognitive domains including those of memory, attention, and executive function. In doing so, it has provided substantial evidence for the neural underpinnings of specific cognitive functions (Fray, Robbins, & Sahakian, 1996); these relationships will no doubt be further elucidated by advances in neuroimaging techniques. By comparing performances of different diagnostic groups, dissociations among specific cognitive abilities have been described which help characterize the relationship between neurological structure and function and the effects of different pathologies on those relationships.

The theoretical basis for the development of the CANTAB, set as it was in the context of animal models of neuropsychological function, has served to yield a battery that can be used across the life span and across all levels of ability. It is sensitive to early changes in cognition, to cognitive decline, and to differences among distinct neuropathological conditions. Further, extensive published research attests to its utility in describing normal cognitive development as well as in measuring pharmacological treatment effects in multiple disease states. The potential for widespread application of the CANTAB to clinical rather than research settings has not, however, been fully investigated. It is possible that as familiarity with computers becomes truly universal across all age cohorts, current barriers, both perceived and actual, to their use with older populations will dissipate. As computerized tests become more ubiquitous in the clinical setting, batteries such as the CANTAB that are based in theory and extensively researched will offer a viable option for comprehensive assessment of cognitive function.

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