The Digit Symbol Substitution Test (DSST) is a quantitative measure of short-term memory and speed of processing used to detect cognitive dysfunction in patients with MDD. The DSST is a 100-item test, each item consisting of a letter paired with a number. The patient is instructed to quickly and sequentially substitute the number with the letter symbol. The test is performed without feedback, with the patient's score being the number of correctly completed symbols within 90 seconds. The DSST can be used to monitor changes in cognitive function over time and can be performed in clinical settings.

**Introduction to the DSST**

- **The DSST is a paper-and-pencil cognitive test presented on a single sheet that requires the patient to copy, into spaces below lines of numbers, the symbols that are matched to each number according to a key located on the top left of the page.**
- Often referred to as “coding” or “symbol coding,” the paradigm of the DSST has survived almost unchanged in its 1939 form to the most recent version (IV) of the Wechsler Adult Intelligence Scale. Comparable versions can be seen in the Brief Assessment of Cognitive Impairment in Schizophrenia (BACIS) and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).
- **The DSST is perhaps the most commonly used test in all of neuropsychology due to its brevity and high discriminative validity; however, the question of “what it measures” still has no definitive answer.**
- Although performance on the DSST is affected by the absolute level of the deficit in the absence of further testing, it is still widely regarded as a clinically useful tool because of its sensitivity to neuropsychological dysfunction in a wide range of clinical populations.
- As a result of the DSST’s high level of sensitivity to general cognitive impairment in a range of brain diseases and conditions (MDD), its value is increased and is widely used in clinical pharmacology trials and clinical practice.

**WHAT CONSTRUCT DOES THE DSST MEASURE?**

- The DSST taps into the human-motor examination as a result of its favorable practical and psychometric qualities, the DSST was incorporated into the original Wechsler Bellevue IQ test battery.¹⁻² Its utility as a clinical tool in neuropsychology became evident when it was shown to reliably distinguish patients with brain damage during the screening of workers.³⁻⁴

- **Good test performance on the DSST requires intact functioning on the attributes of motor speed, attention, visuomotor spatial functions, and scanning, and functions associated with writing or drawing (ie, basic manual dexterity).**

- **Performance on the DSST may also be affected by associative learning: If ratings are rapidly following the first few trials, performance speed will improve because the patient will not need to check the accuracy of each pairing.**

- The decision to consciously engage in this learning strategy to improve performance speeds calls upon the executive functions of planning and strategizing.

- **Working memory—another executive function—is also likely required to keep task rules in mind during the test and for the continuation of updated digit symbol pairings.**

- **Laue and Lennér** noted in their review that DSST is often more highly correlated with verbal measures, suggesting that performance also involves some aspects of written language functioning as well.

- In most populations, digit symbol coding performance is highly correlated with overall cognitive performance. For example, in schizophrenia, Burton et al found 5 principal cognitive domains (ie, processing speed, attention and working memory, and learning) through a factor analysis of the MATRICS Consensus Cognitive Battery that the BACIS symbol coding score correlated with each of these factors at r values exceeding 0.80.

- **Benes and Baron†** evaluated the effect of active training on the DSST as a way of disassembling the cognitive demands of a 30-second DSST were performed every day for 5 days, with new number-code pairs on each trial. In this way, both elderly and young patients improved their scores within each day and between days (Figure 3).

- Because learning of the number-code pairs could only improve performance between related trials, it would seem that associative learning contributes to performance but is not sufficient.

- Hence, it is likely that some other cognitive operation is in force that does improve with practice. Simple motor speed does not typically sustain improvement with practice. The executive function of strategizing or consciously exerting effort to learn is necessary in addition to this.⁵⁻⁶

- **There is good agreement that the DSST is a polyfacial measure whose performance can be dissociated or impaired on a variety of cognitive domains, among which are motor speed, attention, and working memory/ executive functioning, domains that have shown impairment in studies of MDD patients.**

**DSST PERFORMANCE IN PATIENTS WITH MDD**

- Studies have shown neuropsychological performance is impaired in patients with MDD with a 0.5 standard deviation (~1SD) impairment compared to healthy controls and patients with MDD have shown impairment on neuropsychological measures of executive functioning.⁶⁻⁻⁸ Interestingly, the magnitude of DSST performance deficit relative to controls studied in the meta-analysis of 1904 patients (mean±SD age, 50.5±17.8 years) from 22 studies yielded a mean standardized effect size of −0.51.⁸⁻¹⁻² This finding is across the domain of executive functioning as a whole (0.55; p=0.001 [95% confidence interval: 0.34–0.75]).

- **Similar findings were reported in elderly depressed patients (mean±SD age, 70.3±4.7 years), where DSST performance was worse in late versus early onset depression.⁹⁻¹⁻²**

- In patients with MDD (age 18–59 years) who were studied for 6 months after discharge from hospital for an MDD episode, the DSST was strongly associated with the level of functioning achieved in work, school, and home, yielding an odds ratio of 10.95 (scaled to odds units).¹⁻⁴

- A difference of >0.5 on the DSST was associated with a nearly 20-fold increase in odds of obtaining a 1-point better rating on the 7-point global scale of overall clinical improvement (Patient- and Investigator-Facing, an index of real-life functioning in the community.

**CLINICAL RELEVANCE OF CHANGES IN THE DSST**

- The use of the DSST is to change both acutely and chronically [ie, with age] in the same patient it can reveal certain factors in the clinical course that may have implications for cognitive dysfunction (Cognitive dysfunction) and its link to depression (Depressive symptoms) in different subgroups of patients with depression.¹⁻⁴

- **The importance of changes in the level of functioning achieved in work, school, and home, (odds ratio: 0.29; 95% confidence interval: 0.13–0.64) was identified in the current study.**

- Patients who reported a decline in the level of functioning achieved in work, school, and home (odds ratio: 0.29; 95% confidence interval: 0.13–0.64) were more likely to be depressed than those who did not report a decline.¹⁻⁴

- Although the DSST is not specific as to the nature of the deficit in the absence of further testing, it may be similar to impairments observed in elderly depressed patients (mean±SD age, 32 yrs) with depression.¹⁻⁴

- **The DSST has recently been investigated in 2 clinical trials of nortriptyline (an antidepressant for the treatment of MDD) in patients with MDD, with the relative effect compared to placebo highlighted in Figure 4.**¹⁻⁴ The effect of nortriptyline (an antidepressant with multiple indications), utilized as an active comparator in 2 studies,¹⁻⁴ ¹⁻⁵ is also included.

- For a patient to warrant being considered for the subjective experience of a cognitive effect of comparable magnitudes, the second half of Figure 4 shows how changes of this magnitude are associated with clinically meaningful change in performance.¹⁻⁴

**CONCLUSIONS**

- **The use of DSST for clinical decision making in MDD has not been widely tested, but has known sensitivity to cognitive dysfunction (acknowledging the use of this test in 1 study, Bayer et al, reported that concussed symptomatic athletes showed no significant change from baseline, in contrast to non-concussed (control) and concussed (symptomatic) athletes, who displayed significant improvements.**

- In the current study, the clinical meaningfulness of the magnitudes of change on the DSST can be interpreted (using the 10-point Pfeiffer Functional Activities Questionnaire (PFA)), it may be one of many potential tools worth exploring for clinical application.

- The DSST measures a cognitive construct that is sensitive to both baseline and acute effects. This has been shown in sports concussion literature, for example, a study by Negk et al, reported that concussed symptomatic athletes showed no significant change from baseline, in contrast to non-concussed (control) and concussed (symptomatic) athletes, who displayed significant improvements. Hence, for an individual patient, improvement in performance over time is possible even in the absence of an effective treatment.

- Computerized tests sensitive to the cognitive dysfunction observed in MDD may also be useful by reducing or eliminating practice effects, hence making them potentially even more sensitive to clinically meaningful change.

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- For a patient to warrant being considered for the subjective experience of a cognitive effect of comparable magnitudes, the second half of Figure 4 shows how changes of this magnitude are associated with clinically meaningful change in performance.¹⁻⁴

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