Part III

Evaluating cognitive dysfunction in major depressive disorder

Chapter 16

Measuring the mind: detecting cognitive deficits and measuring cognitive change in patients with depression

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Introduction

The focus of this chapter will be the measurement of cognitive change and the detection of cognitive deficits in patients with major depressive disorder (MDD). Whilst this chapter deals specifically with the measurement of cognition in MDD, the principles outlined are equally applicable to other neurological and psychiatric conditions and are offered as guidance for the measurement of cognitive efficacy and safety when testing a variety of putative therapies, including pharmacological, psychotherapeutic, and training/remedial interventions. A full review of the literature dealing with cognitive deficits in patients with MDD is beyond the scope of this chapter, but before progressing to a discussion of detecting deficits and measuring cognitive change we will briefly review the evidence for deficits with reference to recent meta-analyses. An advantage of this focus is that the coinage we will deal in is effect size, a convenient common vocabulary for comparing performance with other diseases and disorders, as well as between cognitive domains and when comparing therapeutic interventions. Later in the chapter we shall employ effect size in our discussion of clinical relevance. We begin with a consideration of human cognition with a focus on its division into various domains, their measurement, and the challenges of obtaining pure measurements of specific domains. For the purposes of clarity we will define cognitive testing as a subset of neuropsychological testing, as this latter category also includes, but is not limited to, the assessment of mood, handedness, etc. Note that we will not employ the term "neurocognitive," which we regard as an unnecessary tautology.

Cognitive domains

Cognitive tests are often described as measures of specific cognitive domains or functions. However, in addition to what can be thought of as the primary domain, almost all tests are to some degree dependent upon intact performance in a variety of auxiliary domains. For example, performance on a word list learning task is reliant on the individual's ability to encode, store, and retrieve new information, but the capacity to encode information is reliant on attentional skills. Also, the new data will pass into working memory (WM) before being encoded into episodic

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memory. Furthermore, successful performance will be reliant on the individual's ability to have understood and remember test instructions, aspects of memory and language. Successful performance on even rudimentary tasks, such as simple reaction time (SRT) tests, requires the individual to focus their attention at the location to which the imperative signal (IS) will be delivered. Furthermore, the setting of an optimal trade-off between speed and accuracy likely requires some decision-making executive functional resources (Henderson, Harrison, & Kennard, 2001). Cognitive tests are labeled as tests of memory, attention, executive function (EF), etc.; however, they are impure as selective measures of these cognitive domains.

The capacity of a test to index a variety of domains can sometimes be a virtue, especially when there is limited time to determine whether the individual being tested has any evidence of cognitive impairment. A class of test generally acknowledged to test multiple domains is variants of coding tasks. A popular example of this paradigm is the Digit Symbol Substitution Test (DSST) from the Wechsler Adult Intelligence Scale (WAIS). In this test individuals are required to draw symbols in paired boxes, the upper box of which contains a number. The correct symbol is indicated in a legend which shows the numbers 1–9, each paired with a unique symbol. The test is helpfully brief (< 2 minutes), easy to understand, and relatively easy to score and administer. Successful performance is reliant upon the functional integrity of a number of cognitive skills, including psychomotor speed, attention, WM, and EF. It is also possible to derive an advantage on this test by learning the number–symbol associations, a function of episodic memory. This task is an effective means of assessing cognitive performance that yields a readily comprehended outcome measure – the total number of symbols correctly completed. However, poor performance on the DSST is not easily accounted for, as it can be due to impairment in one or more of the listed domains. Similarly, positive treatment effects detected with the DSST can be due to possible improvements across the same range of cognitive skills. A method for "dissecting" DSST effects is discussed later in this chapter.

In the foregoing section we have referred to a number of cognitive domains very superficially. In the following subsections we will describe and discuss each of them in detail, preparatory to describing the typical mean level of deficit seen in patients with MDD. We will limit the extent of our discussions to the five listed domains and we will not here consider cognitive domains such as language and praxis. This is not to suggest that these domains are not of interest or significance. However, investigations of possible impairments in these domains have not so far been a particular feature of the literature dealing with cognitive deficits in MDD. Readers interested in the assessment of these functions are directed to the substantial literature on praxis and language to be found in standard neuropsychological testing textbooks (e.g. Lezak, 1995).

Psychomotor speed

Psychomotor speed is often afforded the status of a distinctive domain. However, a reasonable alternative perspective is to regard it more simply as an outcome measure. On this interpretation psychomotor speed is merely the metric employed to measure performance when the task requires a speeded response. When evaluating this skill we are typically most concerned with the study participant's capacity to respond to an environmental event. This typically takes the form of an imperative signal (IS), usually a visual stimulus to the study participant to make a response. A standard paradigm for evaluating this function is an SRT in which an onscreen IS elicits a button press. It must be noted that stimulus appraisal is facilitated by focusing attention at the location to which the IS is expected. Successful completion requires also that the response be prepared ready to "go" on detection of the IS. A further dimension of the task is for the study participant to set a speed/accuracy trade-off criterion. Hence performance on tasks often described as psychomotor speed tasks is typically reliant