SYMPTOM REPORT, DIAGNOSIS AND NEUROCOGNITIVE PERFORMANCE

ABSTRACT

Objective: This second report is concerned with the association between patient self-report generated by a computerized questionnaire with patients' cognitive performance as well as to their specific diagnosis.

Method: The Neuropsych Questionnaire (NPQ) was administered to a large number of patients with different neuropsychiatric disorders to measure their subjective state on the same day that their cognitive state was measured with a comprehensive computerized neurocognitive test battery (VS10). We examined the data of normal subjects and patients in six diagnostic categories: attention deficit hyperactivity disorder (ADD), generalized anxiety disorder (ANX), major depression (DEP), bipolar affective disorder (BPAD), traumatic brain injury (TBI), and cognitive disorders (not ADD or dementia, COG). A method was devised to evaluate the neuropsychological correlates of each disorder relative to cognitive performance and symptom severity.

Results: The correlations between patient symptom self-report and cognitive performance are negative – that is, higher symptom loads are correlated with lower cognitive scores – but they are relatively small. Patient reports of cognitive symptoms are not more highly correlated with cognitive performance than self-reports of manic, anxiety or depressive symptoms. The subjective experience of pain or other somatic symptoms is the strongest correlate of cognitive weakness. In general, tests of complex information processing and effortful attention are the most sensitive to variation in NPQ scores, and symptom scales in the somatic factor of the NPQ are more strongly related to cognitive performance than scales in the mania factor, the anxiety-depression factor or even the cognitive factor.

High functioning (HF) and low functioning (LF) patients in each diagnostic group were defined on the basis of their cognitive performance on acomputerized neurocognitive test (CNT). Patients who are cognitively impaired (LF patients) have a different kind of symptom expression compared to patients who are cognitively intact, and this observation holds for all six diagnostic groups. LF patients have evidence of comorbidity, and a more diffuse pattern of symptom expression, with more symptom scales crossing the threshold of significance. This simple observation has enormous significance, we believe, for the conduct of clinical trials, where symptom expression is central to the evaluation of drug effects; indeed, for any kind of research where patient diagnosis is dependent on patient self-report.

High symptom (HS) and low-symptom (LS) patients in each diagnostic group were defined in terms of their symptom load scores (SLS). Within each diagnostic category, HS patients were compared to LS patients, and each group was compared to the scores of normal subjects. When LS patients differed from normals in cognitive performance, it was assumed that the effect size is a trait indicator. The increase in effect size in HS patients was assumed to be a state indicator. Differences from normal in the LS patients were most likely to be seen in the complex information processing speed and working memory factors. The decrement in cognitive performance in HS patients relative to LS patients was most strongly seen in tests of effortful attention, suggesting it is the most sensitive domain to the severity of the patient's clinical state.

Conclusion: Although the diagnostic utility of patient self report on the NPQ was limited, and correlations with cognitive performance were low, applying HF/LF and HS/LS generated interesting results which may have a bearing on how cognitive research is conducted in neuropsychiatric patients.

SIX DIAGNOSTIC GROUPS

The Neuropsych Questionnaire (NPQ) is a broad-spectrum symptom checklist appropriate for use in patients with neuropsychiatric disorders. It is computerized, freely available over the internet, and can be saved to a database in order to generate serial reports. In previous publications, we have shown that the NPQ is as reliable as the rating scales upon which it is largely based.[1] Although there is some relation between NPQ scores and diagnosis, the relations are not strong, and the discriminant validity of the test, at least with respect to diagnosis, is limited. Like all rating scales, it is vulnerable to the "halo" effect. Although the NPQ contains 20 symptom scores which, in turn, load with four factors, a single metric, the symptom load score (SLS) is highly correlated with the scale and factor scores, and is a useful gauge of the overall severity of the patient's condition.

This report is about the relation of the NPQ to patient's performance on a battery of computerized neurocognitive tests (CNT) administered on the same day. Because the association between cognitive performance and symptom self-report was likely to be different in patients with different diagnoses, we selected six diagnostic groups whose numbers were sufficient to support separate analysis. These were: attention deficit hyperactivity disorder (ADHD), generalized anxiety disorder (ANX), major depression (DEP), bipolar affective disorder (BPAD), traumatic brain injury (TBI), and cognitive disorders (not ADD or dementia, COG).

Cognitive weakness is a component of most, if not all, neuropsychiatric disorders, and cognitive symptoms are the most frequently cited complaints on the NPQ.[1] However, we should have modest expectations when we try to correlate the NPQ to objective measures of cognitive performance. Patient self-report is a notoriously inaccurate gauge of cognitive performance. Much of the relevant research has been in elderly patients. One in three people over 75 might complain of memory problems, but their complaints are poor predictors of performance on neuropsychological tests.[2] In cross-sectional studies of elderly people, subjective memory complaints tend to be associated with depressive symptoms rather than objective impairment.[3 4] In cases of Alzheimer's and Parkinson's disease, patients' perceptions of cognitive impairment are less accurate than caregivers', and the disparity increases with the progression of patients' dementia.[5 6 7] In elderly patients with dementia, the discrepancy between subjective experience and objective performance may be attributable to loss of insight, but similar discrepancies have also been reported in patients with major depression[8], multiple sclerosis[9], fatigue[10] and mild traumatic brain injury.[11] In concussion patients, the correlation between subjective cognitive symptoms and objective performance is modest: in one study, in the range of 0.36 to 0.48[12], and, in another, in the range of 0.31 to 0.51.[13]

Nevertheless, it was reasonable to pursue this line of investigation, because of the comprehensive nature of the NPQ and the CNT we used, and the large numbers of patients whose data were available to study. Computerized data collection in a large neuropsychiatric clinic is conducive to economies of scale that compensate, at least to a degree, for the archival and retrospective nature of the research method and the lack of strict research methodology in the designation and classification of patients. Further, we believe that other methods, beyond correlation analysis, should be applied to vitalize this heretofore fruitless line of inquiry.

The choice of the six diagnoses was not only driven by the number of patients in each category. ADD and TBI have well-defined neurocognitive profiles and a variable pattern of symptom expression. The three psychiatric disorders, ANX, DEP and BPAD have well-defined symptom expression but a variable pattern of cognitive impairment. Patients in the cognitive disorder category are defined by a profile of cognitive weakness in the absence of concurrent psychiatric or neurological disease. This is a broad canvas upon which to test a method.

The three psychiatric disorders are the most appropriate groups to study in this evaluation of the NPQ, because symptom self-report has become, for better or worse, increasingly central to psychiatric diagnosis. Rating scales of symptom intensity are essential to the conduct of clinical trials in patients with these conditions, and even the "semi-structured interviews" that are frequently used are just a more elaborate way to elicit patient self-reports. The NPQ contains 20 symptom scales, 13 of which are psychiatric in nature. (Three are cognitive and four refer to somatic symptom complexes.) Many of the items in the NPQ correspond to items in the various psychiatric rating scales, and the correlations between them are respectable, if not impressive. The NPQ, therefore, ought to generate meaningful information about the characteristics of patients with these three disorders.

Relating the NPQ to cognitive performance in patients with ANX, DEP or BPAD, on the other hand, is a daunting test. In contrast to ADD, TBI and COG, cognitive impairment is not a defining characteristic of anxiety, depression or bipolar disorder. Nevertheless, cognitive deficits are not infrequently met with in patients with the disorders, and numerous studies have tried to discover reliable cognitive correlates. The idea of a "cognitive endophenotype" refers to the possibility that a specific area of cognitive weakness might indicate an underlying proclivity towards the development of the condition. The results of such studies, as we shall discuss, have not been notably successful.

There are a lot of reasons why it has been so hard to establish consistent relationships between psychiatric diagnoses and patterns of neurocognitive ability. Investigators tend to use their own test batteries, for example, and there has never been a standard battery that would allow studies to be reliably compared. Since the correlation among neuropsychological tests is not very high, even tests that measure specific cognitive function like verbal memory, test variance will compromise the comparability of results.

The larger source of ambiguity is the diversity of psychiatric patients, even within what are thought to be well-defined diagnostic groups. For example, we, and others, have shown that the cognitive weakness of patients with anxiety, depression and bipolar disorder is driven almost entirely by a subgroup of patients with gross impairment. When that group is excluded – 20% of patients with anxiety and depression, 30% of bipolar patients – the remaining patients perform almost as well as normals do.[14] In a subsequent study, we showed that depressed patients who were cognitively impaired tended to have more severe disorders; severity defined by the duration of illness, hospitalizations, suicide attempts, etc.[15]

Another problem in the study of patients with psychiatric disorders is the reliance of psychiatric diagnosis, in current practice, on patient self-report, and this brings us back to the relevance of the NPQ. Symptom self-report, as we demonstrated, is of limited value for the purpose of diagnostic classification. In this research, however, we have tested it within already established diagnostic groups, and measured it against an objective criterion – cognitive performance. The results support the validity of the instrument, and generate interesting information about the cognitive correlates of the disorders.

METHOD

SUBJECTS: THE NCNC DATABASE

When a patient is evaluated at one of the Neuropsychiatry Clinics (in Chapel Hill, Charlotte or Raleigh), he or she is routinely administered the VS10 battery, along with rating scales, psychological tests and validity measures, as appropriate. The VS10 data are automatically uploaded into a central database, which is maintained under secure conditions and available only to selected clinicians in the practice. Neuropsychiatric diagnoses are based on a comprehensive examination, of which the VS10 battery is only a part; diagnoses are not made simply on the basis of VS10 scores. Diagnoses are affirmed by review by a research psychiatrist (CTG). They are made on the basis of DSM-IVtr criteria.

TBI patients had sustained a severe traumatic brain injury in the past (GCS <8) but had recovered sufficiently to take the VS10 test battery, a task that requires the intellectual ability of an average 8 year old child. Patients with cognitive disorders had been diagnosed with cognitive disorder NOS or mild cognitive impairment; they did not have a concurrent psychiatric or neurological disorder, they were in good health and they didn't meet criteria for the diagnosis of ADD or dementia. Many of them may have had an undiagnosed learning disability, a mild form of ADD, or an early, preclinical dementing disease, but the evaluation failed to discover a likely cause for their cognitive disorder. The "bipolar" category includes patients with BPAD-I and BPAD-II.

Because the data was generated during patients' initial visit, they were all seeking treatment. Only a small number were in a clinically optimal state, seeking only to continue their present treatment. The severity of their condition at the time of evaluation, and the medications they were taking, were quite diverse.

During the course of the evaluation, patients are also administered the NPQ, which is also uploaded to the NCNC database. The patient is asked to rate his or her symptoms over the past two weeks.

Patients give written informed consent to the use of their de-identified clinical data, including VS10 and the NPQ, for the purposes of research and program evaluation. There is a spot on our website (www.ncneuropsych.com) where patients can rescind that permission at any time.

The database was searched for patients age 18-65 who had taken VS10 and the NPQ on the same day (Table 3a). A larger number of normal subjects and patients with the six diagnoses, age 18-65, who had only VS10 data were used as a comparison group for some of the calculations (Table 3b). (The NPQ has been operational since 2007, VS10 since 2005, so the latter has a much larger database.)

THE NPQ

The NPQ is a computerized questionnaire with 207 items that refer to common symptoms of neuropsychiatric disorders. The NPQ is comprised of 20 symptom scales, 17 of which load on one of four factors (Table 1). The sum of the four factor scores generates a summary score, the "symptom load score" (SLS).

TABLE 1. THE NEUROPSYCH QUESTIONNAIRE

SYMPTOM SCALES		FACTOR
Inattention	ATT	CF
Learning problems	LPx	CF
Memory problems	MEM	CF
Anxiety	ANX	ADF
Panic	PANIC	ADF
Agoraphobia	AGORA	ADF

Obsessions, compulsions	OC	ADF
Social anxiety	SAD	ADF
Depression	DEP	ADF
Hyperactivity-Impulsivity	HIP	MF
Mood instability	MS	MF
Mania	MANIA	MF
Aggression	AGG	MF
Psychosis	PSYCH	MF
Pain	PAIN	SF
Somatization	SOMA	SF
Fatigue	FTG	SF
Disordered sleep	SLEEP	
Suicide	SUI	
Substance abuse	SA	

THE CNS VITAL SIGNS BATTERY (VS10)

The CNS Vital Signs computerized test battery contains seven tests and is widely used by neurologists, psychiatrists and neuropsychologists. VS10 is a research version of the test battery, routinely used in the Neuropsychiatry Clinics and also used in clinical trials and other research projects. The tests in VS10 embrace a broad span of cognitive domains, and are known to be sensitive to most of the causes of mild cognitive dysfunction. VS10 has ten tests that generate 12 independent scores. Eleven of the 12 test scores comprise five factors.

The first factor is *complex information processing* (CIP), and is comprised of three tests. Symbol digit coding (SDC), based on the symbol digit modalities test[16], itself a variant of the Wechsler digit symbol substitution test. The Stroop Test (ST)[17] has three parts that generate simple and complex reaction times. Averaging the two complex reaction time scores from the Stroop test the "response time" (RT) score. The Shifting Attention Test (SAT) measures the subject's ability to shift from one instruction set to another quickly and accurately. Other computerized batteries, like the NES2, CogState and CANTAB have shifting attention tests. Color-shape tests like the SAT have been used in cognitive imaging studies.[18] [19] The SAT score is calculated by subtracting the number of errors from the number of correct responses.

The second factor is *working memory* (WM) and is comprised of two subtests of the Working Memory Test (WMT): a one-back continuous performance test (CPT, WM3) and a 2-back CPT (WM4). In a one-back CPT, the subject responds if the stimulus is the same as the one immediately preceding. In a two-back, the subject responds if it is the same as the one before the preceding stimulus.

The third factor is *effortful attention* (EA) and is comprised of two tests: the number of errors committed during the Stroop test, and a conventional CPT. The Continuous Performance Test is a measure of vigilance or sustained attention. [20]

The fourth factor is *memory* (MEM) and its components are the *v*erbal memory (VBM) and visual memory (VIM) tests. VBM and VIM are adaptations of the Rey Auditory Verbal Learning Test and the Rey Visual Design Learning Test.[21] [22] VBM and VIM are recognition tests, however, not tests of recall. Correct responses from VBM and VIM are summed to generate a composite memory score (MEM).

The fifth factor is *perceptual ability* (PA) and is comprised of two tests. The perception of emotions test (PET); the subject has to match facial expressions with the appropriate word that describes that expression. The

non-verbal reasoning test (NVRT) is similar to Raven's Progressive Matrices or the Matrix Reasoning test on the WAIS. So, perceptual ability is tested in two contexts: social and abstract.

The twelfth test score is finger tapping (FTT). FTT is one of the core tests of the Halstead-Reitan Battery, but similar tests were used by nineteenth century psychologists like Wundt, Galton and Cattell. The FTT loads with complex information processing more than any other factor, but it is more appropriately used as a covariate in the analysis of data from all the other tests. By so doing, one can strip the element of motor speed from the subject's performance; the residue thus left is a cleaner picture of cognitive ability.

The tests generate raw scores and standard scores. Scores are standardized by adjusting for age (on the basis of data from 4400 normal subjects age 6 to 96) to a mean of 100 with a standard deviation of 15. A single summary score, the Index score, is generated by averaging the standard scores of the five factors.

Test-retest reliability and the concurrent validity of VS10 are comparable to similar, conventional neuropsychological tests.[23] The discriminant validity of the CNS VS battery has been established in studies of patients with mild cognitive impairment (MCI) and early dementia[24]; post-concussion syndrome (PCS) and severe traumatic brain injury[25]; ADHD[26 27]; depression[28 29]; schizophrenia and bipolar disorder[30]; and malingering.**Error! Bookmark not defined.**

TABLE 2. VS10

VS10		TIME	FACTOR
Verbal Memory Test	VBM	2.7	MEM
Visual Memory Test	VIM	2.7	MEM
Finger Tapping Test	FTT	2.9	
Symbol Digit Coding Test	SDC	4.2	CIP
Stroop Test (errors)	ST	4.8	EA
Stroop Test (response time)	RT		CIP
Shifting Attention Test	SA	2.7	CIP
Continuous Performance Test	CPT	5.6	EA
Perception of Emotions Test	PET	2.0	PA
Non-verbal Reasoning Test	NVRT	5.0	PA
Working Memory Test (one-back CPT)	WM3	7.0	WM
Working Memory Test (two-back CPT)	WM4		WM
Total Time		39.6	

RESULTS

Records were available for 1127 adult subjects age 18-79 who had taken the NPQ and VS10 on the same day: 42 normal subjects and 1085 patients from 4 diagnostic groups (Table 3). The following demographic variables were covariates in the analyses of variance: age, sex, years of education and self-reported computer familiarity (1 = none, 2 = some, 3 = frequent), gender and race.

TABLE 3. DEMOGRAPHIC CHARACTERISTICS OF THE NPQ/VS10 SAMPLE.

	NML		GAD		MDD		ADHD		BPAD	
N	45		140		345		444		153	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
AGE	35.6	10.9	36.7	12.7	40.8	14.4	30.6	12.0	38.8	12.4
EDUC	15.7	1.9	14.5	2.5	14.4	2.3	14.7	2.2	14.1	2.3
COMPNUM	2.9	0.3	2.8	0.5	2.7	0.6	2.8	0.4	2.7	0.5
SEX % MALE	0.33		0.38		0.34		0.51		0.26	
RACE % WHITE	0.69		0.84		0.79		0.79		0.75	

Correlations Between the NPQ and VS10

In the entire group of 1127, NPQ symptom scores were correlated with cognitive performance scores on VS7. The correlation table (Table 4) shows two characteristics, which are typical of the entire group and of each individual diagnostic group: first, almost all of the correlation coefficients were negative, indicating that lower scores on the cognitive tests were associated with higher symptom scores; second, none of the correlations were high. For example, the correlation between the two summary scores, the SLS and the Cognitive Index was r = -0.273, indicating that only about 7.5% of the variance in one variable was determined by the score on the other. Correlations with the cognitive factor of the NPQ are of particular interest: the correlation coefficients range from -0.12 to -0.22. The average correlation of the 8 cognitive scores with the cognitive factor was -0.18. The average correlation with the somatic factor of the NPQ was -0.21 and with the SLS it was -0.22. This suggests a non-specific association between symptom self-report and cognitive performance; patients performed worse on the cognitive tasks relative to their self-reported somatic symptoms and their overall symptom load.

Table 4. Correlation of NPQ scores with cognitive performance

	INDEX7	MEMs	FTTs	SDCs	STs	RTs	SATs	CPTs
SLS	-.273	-.199	-.177	-.212	-.254	-.133	-.289	-.236
CF	-.216	-.219	-.119	-.134	-.216	-.156	-.208	-.207
MF	-.193	-.147	-.087	-.156	-.223	-.067	-.240	-.180
SF	-.276	-.147	-.228	-.241	-.206	-.114	-.282	-.205
ADF	-.204	-.131	-.134	-.161	-.193	-.083	-.219	-.176
ATT	-.153	-.160	-.062	-.081	-.183	-.113	-.142	-.176
LPX	-.222	-.237	-.131	-.132	-.207	-.166	-.205	-.195
MEM	-.240	-.225	-.150	-.172	-.219	-.165	-.246	-.213
ANX	-.148	-.088	-.068	-.123	-.171	-.058	-.161	-.124
PANIC	-.192	-.113	-.121	-.172	-.160	-.095	-.200	-.173
AGORA	-.214	-.134	-.153	-.148	-.149	-.087	-.209	-.168
OC	-.206	-.165	-.128	-.149	-.211	-.121	-.212	-.169
SAD	-.094	-.085	-.096	-.054	-.095	-.035	-.115	-.076
DEP	-.172	-.090	-.111	-.152	-.176	-.037	-.195	-.166
HIP	-.132	-.134	-.018	-.109	-.207	-.077	-.168	-.114
MS	-.159	-.087	-.077	-.120	-.175	-.038	-.193	-.162
MANIA	-.188	-.144	-.081	-.193	-.206	-.085	-.244	-.161
AGG	-.111	-.083	-.049	-.098	-.138	.001	-.182	-.142
PSYCH	-.199	-.160	-.139	-.130	-.177	-.074	-.202	-.156
SOMA	-.252	-.143	-.183	-.229	-.197	-.119	-.270	-.201
FTG	-.195	-.101	-.175	-.179	-.130	-.075	-.207	-.142
PAIN	-.297	-.155	-.247	-.241	-.235	-.119	-.283	-.212
SLEEP	-.180	-.081	-.110	-.146	-.173	-.058	-.191	-.143
SUI	-.134	-.060	-.104	-.112	-.142	-.014	-.120	-.130
SA	-.011	.006	-.001	-.027	-.011	.060	-.012	-.055

In Table 6, the second column shows the average correlations of the 12 tests. The correlations between the tests and the SLS are in the column on the right. Overall, the SAT is the most highly correlated with symptom load.

TABLE 6. TEST CORRELATIONS, RANK-ORDERED

TEST	AVG	SLS
SATs	-0.186	-.273
STs	-0.149	-.220
CPTs	-0.146	-.219
SDCs	-0.139	-.203
VIMs	-0.138	-.204
SAs	-0.131	-.179
FTTs	-0.124	-.176
NVRs	-0.117	-.138
VBMs	-0.111	-.171
RTs	-0.104	-.151
WM3s	-0.102	-.147

Table 7 is the converse of Table 6, the average correlation of the 12 tests with each of the 20 scales in the second column. In column on the right the correlations between each of the symptom scales and the Index score from VS10. Overall, the pain and somatic scales have the strongest association with cognitive performance.

TABLE 7. SCALE CORRELATIONS, RANK-ORDERED

SCALE	AVG	INDEX
PAIN	-0.216	-.293
SOMA	-0.194	-.270
MEM	-0.186	-.263
AGORA	-0.162	-.233
LPX	-0.154	-.220
OC	-0.148	-.209
MANIA	-0.145	-.196
FTG	-0.142	-.202
PSYCH	-0.140	-.201
PANIC	-0.125	-.185
SLEEP	-0.122	-.166
MS	-0.111	-.155
DEP	-0.111	-.166
AGG	-0.108	-.147
HIP	-0.104	-.126
ATT	-0.100	-.124
SUI	-0.094	-.127
ANX	-0.091	-.112
SAD	-0.083	-.108
SA	-0.052	-.035

In Table 4, it is notable that the cognitive factor (CF) is no better correlated with cognitive performance than the mania factor (MF) or the anxiety-depression factor (ADF). In Table 8, we show examine the correlations between cognitive performance and subjective report in greater detail, the correlations of the test scores with the three cognitive scales (attention, learning problems and memory) and the cognitive factor. The tests that are most highly correlated with the attention scale are the two tests of effortful attention, the CPT and the ST. The tests that are most highly correlated with learning problems are the two memory tests, VBM and VIM. The tests that are most highly correlated with the self-reported memory problems are the SAT and the VBM. These five tests are the most highly correlated with every cognitive symptom scale and with the cognitive factor. Performance on tests of nonverbal reasoning and working memory are least well correlated with the subjective experience of cognitive impairment.

The largest correlation is -0.264, however, indicating that less than 7% of the variance in subjective and objective measures of one's cognitive status are shared.

TABLE 8. TEST CORRELATIONS WITH THE COGNITIVE SCALES AND THE COGNITIVE FACTOR

ATTENTION SCALE		LEARNING SCALE		MEMORY SCALE		COGNITIVE FACTOR	
CPTs	-.150	VIMs	-.214	SATs	-.264	VBMs	-.206
STs	-.146	VBMs	-.204	VBMs	-.245	SATs	-.204
VBMs	-.138	SATs	-.202	STs	-.225	VIMs	-.197
VIMs	-.136	CPTs	-.189	CPTs	-.216	CPTs	-.196
SATs	-.118	STs	-.183	VIMs	-.211	STs	-.196
RTs	-.098	RTs	-.163	RTs	-.189	RTs	-.157
WM4s	-.071	SAs	-.144	SDCs	-.189	SDCs	-.132
SDCs	-.063	FTTs	-.140	FTTs	-.176	FTTs	-.130
SAs	-.063	SDCs	-.130	SAs	-.166	SAs	-.129
FTTs	-.061	WM4s	-.121	WM4s	-.152	WM4s	-.120
WM3s	-.055	WM3s	-.100	WM3s	-.105	WM3s	-.091
NVRs	.049	NVRs	-.052	NVRs	-.090	NVRs	-.028

DISCUSSION

The availability of simultaneous neurocognitive data in a large database of neuropsychiatric patients was the source of the data we report in this paper. The NPQ is a sound instrument, in psychometric terms, but what are the implications of the data it generates? In this report, therefore, our interest moved beyond the NPQ as an instrument; we can be confident that it is a reasonable way to measure patient self-report. Our data, however, indicated that the value of patient self-report, as a diagnostic measure, is limited. Self-report is a necessary measure – one can't imagine undertaking an evaluation without asking the patient what he thinks is the matter. But that information is hardly sufficient, and is only valuable when it is considered in a wider context.

The context of a neuropsychiatric evaluation also includes cognitive testing, so it was appropriate to inquire after the relationship between patient self-report and cognitive performance. We find that they are related: patients who express more severe symptoms on the NPQ tend to perform less well on a computerized battery of neurocognitive tests. They are not, however, very closely related. The correlations are small; the average correlation of the symptom factor scores with the cognitive domain scores is -0.198. This means that only about 4% of the variance in patients' symptoms and cognitive performance are shared. Patients' experience of neuropsychiatric symptoms and their cognitive status are largely independent, and there is no way around having to measure both.

A trivial point, perhaps, and one that has been made many times before, but one only has to look around to see that it flies in the face of common practice. Many physicians who treat ADD patients, for example, rely on patient rating scales. Others prescribe cholinesterase inhibitors to elderly patients simply because they complain of memory problems. The DSM, in fact, at least as some physicians use it, relies in large measure on patient-reported symptoms; the reader is thus cautioned. Symptom self-reports are not sufficient for diagnosing a cognitive disorder. They are relevant to psychiatric diagnosis in the wider sense, but they are not sufficient.

Any further assertions we make about the association between self-report and cognitive function are necessarily compromised by very small correlation coefficients. So, one feels rather like a politician who labors on with a stout expression in the face of anemic polls. We look at the bright side: the fact that all of the correlations between symptom scales and cognitive tests are negative and that almost all are statistically significant. This indicates that that an association exists between patients' performance on the cognitive tests and the severity of their clinical condition, at least in terms of self-reported symptoms. Undeterred by the problem of small numbers, therefore, we sought a measure of coherence.

NON-SPECIFICITY

Unhappily, the most coherent aspect to our correlational data is *non-specificity*. It appears that symptom expression and cognitive performance have a general, not a specific relationship. For example, in the preceding paper, we demonstrated that complaints of cognitive weakness are the most commonly described symptom complex in patients with a number of different neuropsychiatric disorders, including many in which cognitive weakness is not a defining, or even a secondary criterion. In this report we show that patient self-report of cognitive weakness is no better correlated with cognitive performance than self-report of anxiety/depression or manic symptoms, and considerably less well correlated than self-reported pain or other somatic symptoms. In fact, high somatic symptom scores are the strongest correlates of cognitive performance. The SLS, a global measure of symptom load is second strongest.

Two conclusions are possible: that patients who are cognitively impaired are more expressive of neuropsychiatric symptoms in general, and especially somatic symptoms; or we can take these data to mean that patients who are very symptomatic, and especially patients who are experiencing physical symptoms, are more impaired. But which is the more accurate statement? Do severe symptoms drive cognitive impairment or does cognitive impairment amplify one's experience of neuropsychiatric symptoms?

Correlation analysis is not suitable for addressing that question. Correlations speak only to associations, and associations can be the consequence of multiple factors and complex pathways. The question of "drivers" implies a linear relationship between self-report and cognitive performance, a kind of relation that is not very likely either in brain science or human psychology. Indeed, if only about 4% of the variance in two human characteristics are shared, the remaining 96% leave ample room for "multiple factors and complex pathways."

Neuropsychiatrists, though, are used to more specific associations. After all, the essence of neuropsychological testing is that cognitive functions are specific. The original theory behind neuropsychological testing was cerebral localization; the idea that specific functions were the domains of specific brain regions, a principle that was supported by lesion studies in humans and in animals. The modern synthesis is a bit less specific: it relates cognitive functions to complex functional systems that are more or less distributed in cortical and subcortical regions, a principle that is broadly supported by imaging technology, and supported, at least to a degree, in the study of various neurological conditions. Symptom self-report, however, does not enjoy much specificity at all in its relation to cognitive function. What we see in our data is a relatively non-specific relationship based on severity; the most potent correlate of cognitive weakness is what we might call "distress"; and somatic distress is the most cogent of all.

The problem of non-specificity is something that has bedeviled research in this area for a long time. Neuropsychiatric disorders do not behave like cortical lesions in terms of their impact on neuropsychological tests. That may be because neuropsychiatric disorders like ADD, depression, anxiety and bipolar disorder are largely defined in terms of symptom self-report.

THE SPECIAL PROPERTIES OF CNT'S

If we turn our attention to specific tests, we note that, of all the tests in VS10, the SAT is the most sensitive test to the patient's subjective state. The SAT is a measure of cognitive flexibility that loads with the complex information processing factor (CIP). Speaking in more general terms, tests of CIP and EA are the most sensitive to variation in NPQ scores. One might expect memory to be a more sensitive function; after all, patients with cognitive dysfunction complain that their memory is failing, more often than any other cognitive symptom (except perhaps dysnomia). Our data suggest that they may be getting it wrong. The SAT, ST and CPT are as highly correlated, or more so, than the memory tests, to patients' self-reported symptoms of poor memory. Overall, cognitive slowing and inattention/distractibility are the strongest correlates of symptom load, whether symptom load is expressed by the SLS or the cognitive factor or the symptom scales.

Before one makes too much of this observation, it is necessary to consider the nature of the neurocognitive tests that we are using here. Computerized tests are as reliable as conventional neuropsychological tests, and their concurrent and discriminant validity equal to that of conventional tests.[31] In our opinion,however, too much has been made of the fact that computerized tests are correlated with conventional tests, on the order of *rho* = 0.4 - 0.6. In studies like this one, one ought to give as much attention to the differences between CNT's and conventional tests, which shouldn't be attributed simply to "test variance" when something systematic may be at play.

For example, computerized tests are run on a tight clock, so it is hardly a surprise that processing speed is central to good performance. That is probably why on VS10, the Stroop test and the shifting attention test, two

ostensible measures of executive function, load with coding in the CIP factor. Further, in CNT, there is no tester present who can maintain the patient's focus, or ease off when he or she grows weary; so it is no surprise that effortful attention is also a key element of performance. Such problems, intrinsic to CNT, cannot be resolved here. How important they are we shall see, when we compare our results to those generated in studies using conventional tests.

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