References

1. Steffen R. Travel medicine — prevention based on epidemiological data. *Trans R Soc Trop Med Hyg* 1991;85: 156-62.
2. Croft AM, World MJ. Neuropsychiatric reactions with mefloquine chemoprophylaxis [letter]. *Lancet* 1996;347:326.
4. Sturchler D, Handschin J, Kaiser D, Kerr L, Mittelholzer ML, Reber R, et al. Neuropsychiatric side effects of mefloquine [letter]. *N Engl J Med* 1990; 322:1752-3.
4. Hollister LE, Trevino ES. Calcium channel blockers in psychiatric disorders: a review of the literature. *Can J Psychiatry* 1999;44:658-64.

Clozapine and sialorrhea: update

Among the frequently reported side effects of clozapine is nocturnal hypersalivation (sialorrhea), a troubling and potentially hazardous reaction. Hypersalivation can also occur in the daytime, causing social withdrawal and isolation because of embarrassment and stigma.

Many interventions have been used to alleviate this side effect, including dose reduction, addition of antiparkinsonian agents such as benztropine and procyclidine, and use of sugarless candy. For the most part, these interventions work at the systemic level and have not provided any real relief.

As reported in the May 1999 issue of the *Journal of Psychiatry & Neuroscience*, atropine eye drops were tried as a possible intervention.[1] One drop of 1% solution was given sublingually at bedtime, and the dose was titrated as required to achieve maximum relief of symptoms. We reported encouraging results from this intervention.

The use of atropine eye drops to treat clozapine-induced sialorrhea appears to have a beneficial effect despite the presence of an anticholinergic action. However, patients reported that the atropine was short acting and that they experienced rebound sialorrhea in the early hours of the morning, which necessitated repeat dosing. Some patients reported difficulty manipulating the dropper to ensure the proper dosing. The potential for accidental overdose with drops as opposed to a metered spray was worrisome as well. We therefore have looked for other alternatives to atropine eye drops.

Ipratropium bromide (Atrovent) nasal spray is a powerful, longer acting anticholinergic drug that can also be applied sublingually. The spray formulation comes in 2 concentrations: 0.03% and 0.06%. We have been working with the 0.03% solution, normally used to relieve side effects of severe rhinitis, and have found that 2 sprays of this solution under the tongue at bedtime is as effective, if not more effective, than the 1% atropine eye drops in controlling sialorrhea.

Ten patients, formerly receiving atropine eye drops, were successfully switched to ipratropium bromide nasal spray, 0.03% solution, over 6 months. In 2 cases, use of the nasal spray was started directly. Patients reported reduction or resolution of nocturnal hypersalivation after using the spray. Two patients used the preparation twice a day, the remainder only once a day. There were no side effects other than 2 patients reporting that they did not like the taste. Compared with the eye drops, the metered spray was reported to be easier to use and to require less digital precision. In addition, patients were more accepting of carrying the spray with them and using it in public places.

Although further study is required, we find these observations encouraging in the treatment of clozapine-induced sialorrhea. A protocol for studying the effectiveness of this intervention is currently being submitted to an ethics review board for approval.

Pierre Tessier, MD
Carolyn Antonello, RN
Ottawa, Ontario, Canada

Reference

1. Antonello C, Tessier P. Clozapine and sialorrhea: a new intervention for this bothersome and potentially dangerous side effect [letter]. *J Psychiatry Neurosci* 1999;24(3):250.

A short form of the Wisconsin Card Sorting Test

There has been a proliferation of studies of cognitive changes with antipsychotic medications since clozapine was reintroduced to clinical practice 10 years ago, and recent reviews have indicated the extraordinary value of cognitive improvement to sociovocational rehabilitation.[1-3] However, the cognitive test batteries remain too long and complicated for general clinical application, discouraging to both clinicians and patients. In our clinic, we are identifying a series of relatively simple but standardized psychometric tests capable of detecting changes from treatment. In this pursuit, we have examined a short form of the Wisconsin Card Sorting Test (WCST)[4] and have found promising results.

Myriad cognitive impairments are associated with schizophrenia, but most would agree that executive function deficits are a leading barrier to vocational reintegration.

The WCST is particularly sensitive to frontal-lobe lesions[5] and is a well-validated neuropsychological tool for the assessment of executive functioning.[6] The test involves individual presentation of up to 128 cards and requires the examinee to learn simple perceptual rules for classification on the basis of verbal feedback to their responses. Patients with schizophrenia show reliable deficits that imply a predominant frontal-lobe dysfunction.[7-9]

Despite the benefits of the WCST, it requires 30 to 60 minutes to administer and is particularly difficult for patients with schizophrenia who invariably find it to be a demoralizing experience and may reject the test outright. In comprehensive test batteries, the issue of missing data because of test rejection is commonly managed by either prorating scores or by excluding the case record. Although the former is a weak solution on statistical grounds, the latter can be very expensive, particularly in prospective 1-year investigations for which months of data can be lost by rejection of a single test at a single time.

We have intentionally positioned the WCST at the end of our test batteries to ensure that all other data are collected before the WCST is administered. This has worked well, but it introduces a potential positioning bias to our results that may be influenced by extraneous factors, such as fatigue. A preferable option is to modify the WCST so that the important test characteristics are not sacrificed and the test is less frustrating to the patient. Various modifications to the administration method have been proposed,[10-12] but there are insufficient normative data to support their use, and the modifications may result in an instrument not directly comparable to the full 128-item WCST.

Another approach has been to administer the 128-item WCST according to the guidelines of Heaton and associates[4] but to discontinue the test after 64 items. This approach may have merit, and it has been applied in 2 prior investigations that included patients with schizophrenia,[12,13] but, as yet, the normative data currently available from direct applications of the 64-item version have been limited to small and preliminary samples of control subjects.[14-16] Normative data are essential for derivation of standardized scores for the WCST, which are in turn required for the computation of an executive domain score or a general cognitive index score in studies with broader test batteries. These derivations are in turn important for successful prospective examinations of medication effects on cognitive skills.[1,2]

In lieu of normative data, we have examined statistical adjustments to the results of a 64-item version that may allow an interim method for obtaining a proxy measure of scores standardized using the original 128-item normative data. A short-form adaptation of the WCST has been examined in 3 prior studies of mixed psychiatric and neurological disorders.[12,13,17] The first study showed that the number of categories completed with 64 items was not well correlated with the categories completed with 128 items ($r = 0.73$), but the perseverative error score from the 2 versions fared better ($r = 0.84$).[12] The second study showed better correlations between the 64-item and the 128-item versions, but it also found statistically significant differences between the percent scores derived from each method.[17] The third study examined a subset of the variables available from the 128-item norms and found good correlations and no significant differences between the 2 versions.[13] These 3 studies thus provide some preliminary support for the use of a short form of the WCST, but they did not provide data with specific relevance to the utility of the 128-item normative data for adjusting the 64-item variant applied specifically to schizophrenia samples.

Unlike the earlier studies, our assessment included a larger sample of schizophrenia patients, and we will report on the value of several measures, standardized using the 128-item normative data of Heaton and associates.[4] We administered the 128-item WCST to 104 patients with schizophrenia and scored the first 64 items alone before scoring the entire 128-item test. Responses were scored for all published variables except for the number of trials to the first completed category (which is equivalent in the 2 variants), the learning-to-learn score (which requires a minimum of 3 completed categories, rarely achieved in the 64-item version) and the total number of trials administered (which was always 64 in the short version). The total number of categories achieved, failure to maintain set and the total number of correct responses were compared after multiplying the 64-item score by 2 and then using the 128-item normative data to derive standardized scores. A similar procedure was used for total errors, perseverative errors, nonperseverative errors and perseverative responses. These last variables were also converted into percent scores

Table 1: Comparison of 64-item and 128-item Wisconsin Card Sorting Test (WCST) in sample of 104 schizophrenic patients*

Variable	Mean score (and SD) WCST-128	WCST-64	z score WCST-128	z score WCST-64	Pearson correlation, r†	t statistic‡	p value
No. of categories achieved	3.41 (2.19)	2.13 (1.50)	−2.22 (2.37)	−1.31 (3.09)	0.87	5.89	< 0.001
Total no. of errors	48.96 (26.47)	25.47 (12.47)	1.99 (1.76)	2.11 (1.66)	0.82	1.25	0.215
No. of perseverative errors	29.49 (21.62)	14.93 (10.46)	1.85 (1.73)	1.81 (1.74)	0.90	0.39	0.694
No. of nonperseverative errors	20.34 (15.52)	10.54 (7.40)	1.33 (1.97)	1.43 (1.88)	0.88	1.02	0.310
No. of perseverative responses	34.99 (28.70)	17.75 (14.24)	2.67 (3.04)	2.72 (2.98)	0.90	0.39	0.696
Failure to maintain set	1.12 (1.34)	0.60 (0.84)	0.58 (1.33)	0.64 (1.68)	0.70	0.46	0.643
Total no. of correct responses	65.73 (17.05)	38.24 (13.00)	−0.32 (1.79)	0.99 (2.98)	0.52	−5.26	< 0.001
% total errors	40.22 (19.00)	39.80 (19.48)	1.85 (1.73)	1.81 (1.74)	0.83	0.48	0.633
% perseverative errors	24.25 (16.52)	23.36 (16.37)	2.68 (2.99)	2.51 (0.29)	0.92	−1.40	0.166
% non-perseverative errors	16.69 (11.55)	16.47 (11.56)	0.98 (1.63)	0.95 (1.62)	0.85	0.36	0.720
% perseverative responses	28.64 (22.24)	27.73 (22.24)	2.72 (3.27)	2.59 (3.26)	0.91	1.01	0.316
% conceptual level responses	47.17 (25.86)	48.64 (26.37)	−1.91 (1.72)	−1.80 (1.71)	0.91	1.52	0.131

Note: SD = standard deviation.
*Male = 81, female = 23; right-handed = 93, left-handed = 11; mean age = 33.28 years (SD 10.47); mean education = 11.59 years (SD 2.76); mean age of onset = 23.14 years (SD 8.05); mean illness duration = 9.83 years (SD 8.91); premorbid intelligence (estimated with the Peabody Picture Vocabulary Test) = 87.39 (SD 18.24); chart diagnoses of schizophrenia (n = 96), schizoaffective disorder (n = 3) and schizophreniform disorder (n = 5) were not additionally validated in the hope that these results would be applicable to the general population of patients with schizophrenia.
†$p < 0.001$ for all variables.
‡Degrees of freedom = 103 for all variables.

based on the number of items completed (i.e., 64 items in the short version and up to 128 items in the long version), and again the 128-item normative data were used to obtain standardized scores.

The reliability of our estimates, assessed by computing the correlation between the 64- and 128-item variables, and the validity of our estimates, assessed by paired t-test comparisons, are summarized in Table 1. The reliability of the 64-item test was supported by the statistical significance of all correlation comparisons ($p < 0.001$) and the high correlation values of all variables ($r > 0.80$) except for the total number of correct responses ($r = 0.52$) and the number of failures to maintain set ($r = 0.70$). The validity of the 64-item variant was also supported by the absence of significant differences between the derived z scores for all variables except the total number of categories achieved ($t = 5.89$, $p < 0.001$) and the total number of correct responses ($t = -5.26$, $p < 0.001$). There were no substantial differences between the reliability or validity of the standardization scores derived from the multiplication of the 64-item score by 2 or the percent scores.

In this group of patients with schizophrenia, we observed good reliability and validity of the 64-item variant of the WCST standardized with the 128-item normative data. The exceptions to this general conclusion pertained to the poor reliability and validity of the total number of correct responses, the relatively poor reliability of the number of failures to maintain set and the poor validity of the total number of categories completed. Additional investigation will be required to examine the validity of the 64-item variables as markers of frontal-lobe dysfunction. The present data suggest that there is merit in such a pursuit. Also, our correlations were slightly higher than those of prior reports from mixed patient samples, which suggests that the 64-item version may be of greater value in schizophrenia samples than in other patient groups. This, too, will require independent verification.

Scot E. Purdon, PhD
Barbara Waldie, BSc
Edmonton, Alberta, Canada

References

1. Purdon SE. Cognitive improvement in schizophrenia with novel antipsychotic medications. *Schizophr Res* 1999; 35:51-60.
2. Purdon SE. Measuring neuropsychological change in schizophrenia with novel antipsychotic medications. *J Psychiatry Neurosci* 2000;25:108-16.
3. Green MF. Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the "right stuff"? *Schizophr Bull* 2000;26:119-36.
4. Heaton RK, Chelune GJ, Talley JL, Kay GG, Curtiss G. *Wisconsin Card Sorting Test manual: revised and expanded.* Odessa (FL): Psychological Assessment Resources; 1993.
5. Milner B. Effects of different brain lesions on card sorting. *Arch Neurol* 1963; 9:100-10.

6. Lezak MD. *Neuropsychological assessment*. 3rd ed. New York: Oxford University Press; 1995.

7. Saykin AJ, Gur RC, Gur RE, Mozley PD, Mozley LH, Resnick SM, et al. Neuropsychological function in schizophrenia: selective impairment in memory and learning. *Arch Gen Psychiatry* 1991;48:618-24.

8. Saykin AJ, Shtasel DL, Gur RE, Kester DB, Mozley LH, Stafiniak P, et al. Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. *Arch Gen Psychiatry* 1994;51: 124-31.

9. Sullivan EV, Mathalon DH, Zipursky RB, Kersteen-Zucker Z, Knight RT, Pfefferbaum A. Factors of the Wisconsin Card Sorting Test as measures of frontal-lobe function in schizophrenia and chronic alcoholism. *Psychiatry Res* 1991;46:175-99.

10. Nelson HE. A modified card sorting test sensitive to frontal lobe defects. *Cortex* 1976;12:313-24.

11. Means LR, Boake C. Stability and sensitivity of Wisconsin Card Sorting Test short forms. *Clin Neuropsychol* 1994;9:356.

12. Robinson LJ, Kester DB, Saykin AJ, Kaplan EF, Gur RC. Comparison of two short forms of the Wisconsin Card Sorting Test. *Arch Clin Neuropsychol* 1991;6(1-2):27-33.

13. Smith-Seemiller L, Franzen MD, Bowers D. Use of Wisconsin Card Sorting Test short forms in clinical samples. *Clin Neuropsychol* 1997;11:421-7.

14. Axelrod BN, Jiron CC, Henry RR. Performance of adults aged 20 to 90 on the abbreviated Wisconsin Card Sorting Test. *Clin Neuropsychol* 1993;7:205-9.

15. Axelrod BN, Henry RR, Woodward JL. Analysis of an abbreviated form of the Wisconsin Card Sorting Test. *Clin Neuropsychol* 1992;60:27-31.

16. Haaland KY, Vranes LF, Goodwin JS, Garry PJ. Wisconsin Card Sort Test performance in a healthy elderly population. *J Gerontol* 1987;42:345-6.

17. Axelrod BN, Paolo AM, Abraham E. Do normative data from the full WCST extend to the abbreviated WCST? *Assessment* 1997;41:41-6.