The Construct Validity of Root-Mean-Square Error for Quantifying Smooth-Pursuit Eye Tracking Abnormalities in Schizophrenia

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Introduction

Smooth-pursuit eye tracking abnormalities have been consistently observed among schizophrenia patients and their relatives (Iacono and Clementz 1993; Levy et al 1993). Using a statistical technique called mixture analysis, recent studies have demonstrated that distributions of both the patients’ and their relatives’ ocular motor data are best characterized by two distinct components (Blackwood et al 1991; Clementz et al 1992; Gibbons et al 1984; Iacono et al 1992; Ross et al in press; Sweeney et al 1993). One component overlaps the scoring distribution of normal subjects fairly closely, whereas the other component captures subjects with poor eye tracking performance. The pattern of results suggests that ocular motor measures are capturing differences in kind among schizophrenia subjects, and that these differences are indexing biologically distinct subgroups of patients in whose families ocular motor abnormalities are an indicator of vulnerability for some form of this illness. This conclusion is consistent with a report suggesting linkage between eye tracking abnormalities and markers on chromosome 6 (Arolt et al 1995; see also Wang et al 1995).

The above results, which rely primarily on “global” measures of eye tracking performance, should be considered in light of current trends to use “specific” measures, such as saccadic performance and the calculation of smooth pursuit gain, to quantify ocular motor proficiency. Specific measures are helping us understand the neuropathology associated with ocular motor performance deviations among schizophrenia patients (e.g., Clementz et al 1994). Data supporting the use of global measures in schizophrenia research, however, particularly in family studies, are overwhelming. To illustrate this point, we will focus on the value of one global measure, root-mean-square error (RMSE), which provides an index of the extent to which the eyes do not reproduce target motion. Our discussion most likely generalizes to the use of other measures that are mathematically related to and highly correlated with RMSE (Iacono and Clementz 1993).

Many studies attest to the construct validity (Cronbach and Meehl 1958) of RMSE as a measure of eye tracking abnormalities among schizophrenia subjects. RMSE correlates highly ($r \sim .90$) with alternative measures of tracking proficiency among schizophrenia subjects (Iacono and Clementz 1993), has high short- and long-term reliability among schizophrenia (Gooding et al 1994) and normal (Iacono and Lykken 1981) subjects, and differentiates remitted schizophrenia patients from normals (Iacono et al 1981), schizophrenia patients from subjects with other psychoses (Iacono et al 1992), and the relatives of schizophrenia patients from the relatives of patients with other psychoses (Iacono et al 1992). RMSE is also associated with neuropsychological measures that assess frontal lobe dysfunction among schizophrenia patients (Katsanis and Iacono 1991), is related to other putative biobehavioral indicators of schizophrenia (Grove et al 1991), and is correlated with the presence of social–interpersonal, but not cognitive–perceptual, schizophrenia-related clinical features among schizophrenia patients’ relatives.
(Clementz et al 1992). Of the six studies showing that smooth-pursuit performance among schizophrenia subjects reflected a mixture of two distributions, four used RMSE (Clementz et al 1992; Iacono et al 1992; Ross et al in press; Sweeney et al 1993). In all four studies, the characteristics of the two mixing components (separations between groups, proportion of patients in the two components) were highly similar. RMSE scores also fit a genetic model consistent with major gene transmission among schizophrenia families (Grove et al 1992). No other measure of ocular motor abnormalities among schizophrenia subjects has this level of construct validity.

A study questioning the construct validity of RMSE for schizophrenia research (Sweeney et al 1993) stated that findings of mixtures of two component distributions for RMSE scores reflected "measurement artifact." Sweeney et al viewed RMSE as a "composite" of at least two eye movement abnormalities: anticipatory saccades (AS; a type of large saccade that moves the eyes well ahead of the target) and low-gain (slow) pursuit. They hypothesized that mixture in RMSE distributions does not suggest the presence of two biologically different schizophrenia subgroups unless AS and/or pursuit gain also demonstrate mixture. Sweeney et al concluded that their hypothesis was supported by the following findings: 1) RMSE demonstrated mixture among schizophrenia patients; 2) neither AS frequency nor pursuit gain demonstrated mixture among schizophrenia patients; 3) AS, which account for large amounts of spatial tracking error, contributed disproportionately to RMSE scores among schizophrenia subjects, suggesting that they were driving findings of mixture among schizophrenia patients in an artificial manner; and 4) patients in both components were more deviant than normal subjects on ocular motor performance.

Sweeney et al (1993) hypothesized that not finding mixture for AS and pursuit gain indicated that mixture for RMSE was an artifact of the effects AS and/or pursuit gain have on RMSE. This thesis suggests that mixture for a global measure must be paralleled by mixture in the distribution(s) of specific measures that account for some of the global measure's variance. Sweeney et al's hypothesis can be refuted by an example from the classical statistics literature. In his discriminant analysis manuscript, Fisher (1936) presented data on sepal (the green, leafy part of a flower) length and width of two iris species. Using Fisher's statistical technique, we formed a combination of these two variables (creating a "global" sepal variability score) that maximally discriminated the two species. As can be seen from Figure 1, the global score distribution shows statistically significant mixture, each component capturing a different iris species, but the specific measures of sepal length and width do not show mixture. This situation is analogous to that for RMSE, AS, and pursuit gain, and demonstrates that specific measures need not show mixture for a global measure, which is partially a composite of the specific measures, to capture biologically meaningful group differentiations.

Sweeney et al (1993) also hypothesized that mixture in RMSE distributions was an artifact reflecting the "very strong influence of large anticipatory saccades" on RMSE. First, AS size was not measured by Sweeney et al. Second, of the six studies comparing schizophrenia and normal subjects on AS frequency that were summarized by Levy et al (1993), not one found a significant difference, and two reported AS to be rare events. Additionally, Ross et al (in press) demonstrated mixture of RMSE among schizophrenia patients who generated no AS. Third, the pattern of correlations between RMSE, AS, and pursuit gain presented by Sweeney et al refute this hypothesis unambiguously. The correlations between RMSE and AS for normal (r = .58) and schizophrenia (r = .56) subjects were not significantly different. If AS frequency was driving mixture in RMSE distributions, given these correlations, mixture might have been expected among both groups of subjects. The correlations between AS and pursuit gain for normals (r = -.12) and schizophrenia (r = -.50) subjects were significantly different. These results suggest that a combination of high AS frequency and low-gain pursuit determines which schizophrenia subjects have high RMSE scores. Neurological diseases are characterized by combinations of ocular motor abnormalities, not by discrete individual devia-

Figure 1. The distribution of “total sepal variability” (top panel), sepal length (middle panel), and sepal width (bottom panel) for the iris data used by Fisher (1936). Total sepal variability was best characterized (statistically) as a mixture of two nonskewed Gaussian distributions. Sepal length and sepal width were both best characterized as single, nonskewed Gaussian distributions.
tions (see Pierrot-Deseilligny 1994). A plausible hypothesis is that the presence of AS and low-gain pursuit among high-RMSE schizophrenia subjects are pleiotropic manifestations of the same neuropathology. Perhaps global measures like RMSE have worked because they aggregate those abnormalities into a single score among schizophrenia subjects.

Finally, Sweeney et al (1993) concluded that "mixture in RMS error scores does not differentiate groups of schizophrenic patients who have eye movement abnormalities from those who do not" because both of their schizophrenia groups were more deviant than normal subjects on ocular motor performance. We attempted to replicate this finding using Grove et al's (1992) RMSE data from 177 normal subjects (RMSE M = 2.07, SD = 0.23). 72 schizophrenia patients captured by the low-RMSE mixture component (M = 2.05, SD = 0.18), and 20 patients forming the high-RMSE component (M = 2.62, SD = 0.12). Grove et al's high-RMSE patients differed significantly from the other two groups, but, contrary to Sweeney et al, there was no difference between the low-RMSE patients and the normal subjects. Comparing the two data sets suggests the source of this discrepancy. The schizophrenia patient RMSE data from Grove et al and from Sweeney et al (low-RMSE component M = 2.07, SD = 0.15; high-RMSE component M = 2.60, SD = 0.15) were remarkably similar, but Sweeney et al's normals (RMSE M = 1.99, SD = 0.17), composed at least partly of hospital staff, had significantly lower (better) RMSE scores and significantly smaller RMSE variance than Grove et al's normals, a community-based sample. This suggests that Sweeney et al (1993) used a "supernormal" comparison sample, and calls into question their conclusion that low-RMSE patients have abnormal ocular motor performance.

In conclusion, RMSE appears to be a biologically meaningful measure of eye tracking performance with the potential to identify vulnerability for illness among a subgroup of schizophrenia families. It has been, and continues to be, a valuable measurement tool for those studying smooth-pursuit eye tracking in schizophrenia.

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References


