

LACK OF RELATIONSHIP OF NEUROLEPTIC DOSE AND BLOOD SERUM LEVELS TO NEUROPSYCHOLOGICAL PERFORMANCE ON THE LNNB IN CHRONIC SCHIZOPHRENIA

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The relationship of neuroleptic dose and blood serum levels to performance on the Luria Nebraska Neuropsychological Battery in chronic schizophrenics was assessed. Thirty chronic schizophrenics were individually administered the LNNB and a small sample of blood was obtained. No significant correlation between neuroleptic serum levels and test performance in these subjects was found although different conversion formulas related differentially to the blood serum levels.

Keywords: LNNB, schizophrenia

Studying schizophrenia from a neuropsychological perspective can be difficult due to pharmaceutical confounds. Since neuroleptics are often prescribed to chronic schizophrenics to reduce the symptoms of schizophrenia (Baker, Kirsch, Waldo, Bell, Adler, Hattox, Murphy, & Freedman, 1991) understanding the potential relationship of these compounds to neuropsychological performance would be valuable. Traditionally, the effects of neuroleptics on behavior have focused on dose-response-curves. However, research (Tune, Creese, De Paulo, Slavney and Coyle, 1980) has indicated that dosage is not a good predictor of clinical state in psychiatric populations. Indeed, relationships between these two variables were considered to be essentially random (Moulin, Davy, Debruyne, Andersson, Bigot, Camsonne, and Poilpre, 1982). In an effort to determine the efficacy of these pharmaceutical agents on behavior, Tune and colleagues (1980) developed a radioimmunoassay that quantifies blood serum chlorpromazine equivalents. Since the introduction of the radioreceptor assay technique for quantifying serum neuroleptic concentrations in 1977, the technique has been modified to provide researchers with greater precision and sensitivity (Rao, 1986). Early findings from his laboratory showed that blood serum levels, not neuroleptic dose, were most predictive of clinical state and improvement (Tune et al., 1980).

These studies have exclusively used nonparametric variables to assess clinical state. For example, studies by Tune et al. (1980) and Reinikainen, Koponen, Jolkkonen, and Reikkinen (1990) assessed clinical state using the Brief Psychiatric Rating Scale (BPRS).

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While the BPRS is considered to be a useful clinical tool, the validity and reliability of this instrument has not yet been defined. Thus, more standardized test protocols would allow for resolution of this confound. Especially critical to the problem is the issue of replicability. Instruments such as the BPRS limit the ability of different investigators to assess similar behaviors as well as replicate findings. To complicate matters, this instrument does not address effects of neuroleptics on brain functioning and/or dysfunction. In summary, instruments such as the BPRS focus on overt behavior, ignoring specific manifestations of neuropsychological function.

The present investigators were specifically interested in determining whether dose levels were related to blood serum levels, and, in turn, whether either of these two measures were related to neuropsychological performance. Despite the fact that criticisms have been raised against the Luria Nebraska Neuropsychological Battery (LNNB) (Golden, Hammeke, & Purish, 1980), the LNNB was used because of its standardized, broad-based approach to neuropsychological assessment as well as its general popularity in mental health settings. Similar studies in the past have also used the LNNB to measure functioning in chronic schizophrenics (Golden, Graber, Moses, Zatz, 1980; Moses, 1983; Shelly and Goldstein, 1983).

METHOD

Subjects

Thirty right-handed inpatient volunteers from a 1,000 bed state hospital participated in the study. Of these, there were 27 males and 13 females with 17 African-Americans and 13 Caucasian participants. The mean age of participants was 38.7 (SD = 12.39), while mean educational attainment was 9.0 (SD = 3.2). Participants were hospitalized an average of 4.6 times (SD = 4.55) and were currently hospitalized for a mean of 1,641 days (SD = 2667.29). The average age of onset of their respective symptoms was 18.33 years of age (SD = 7.55). All subjects were diagnosed as being schizophrenic by a board-eligible or a board-certified psychiatrist using DSM-III criteria. Diagnoses were independently confirmed by a licensed psychologist via interview and review of records. Twenty-six were diagnosed as chronic undifferentiated, three as schizoaffective and one as paranoid. All subjects had good corrected or uncorrected vision.

Procedure

Inclusion in the study was determined after the purpose of the study was explained and subjects had verbally agreed to participate. All participants then read and signed an informed consent.

Volunteers were escorted to the laboratory where 10 ml blood samples were collected in untreated tubes by licensed laboratory technicians. Samples were allowed to clot at room temperature, centrifuged and then frozen at -20°C . Serum neuroleptic levels were then obtained.

Since subjects were on nine different medications and a wide variety of medication regimens, doses were converted to chlorpromazine equivalents (CPZE) using four well researched conversion formulas (Davis, 1976). Dose equivalence conversions were completed according to published specifications. Twenty-three of the thirty subjects' levels

were converted because six patients were on Navane and one on Serentil, two drugs which were not in existence when the conversion formula was published (Tune et al., 1980).

After blood samples were drawn, subjects were individually administered the 269 items of the LNNB-Form I (Golden et al., 1980). Testing was completed by a research technician trained in neuropsychological assessment who was blind to subject history and/or diagnosis. Testing occurred in the lobby of the subjects' ward. Scores were transformed to *t* values across the 14 major LNNB scales, as outlined by Golden et al. (1980) and copied onto floppy disks via an Apple IIe. After testing was completed, subjects were briefed as to their participation and then escorted back to their ward.

RESULTS

Pearson product-moment correlations were computed between each of the four conversion formula values and blood serum levels in order to determine the relationship efficacy of the formulas to metabolized drug levels. The correlations ranged from .05 to .49. The latter correlation approached the .01 significance level. Considering the number of correlations performed, the .01 level of significance was adopted. For purposes of further analysis, only the Davis (1976) formulas were used since these were ascertained to be the most common and most statistically robust formulas respectively.

When the scores were broken down into drug categories, differences were noted in the correlation to blood serum with strong positive correlations between blood serum levels and butyrophenones, phenothiazine and lithium (.62 to .76) but low negative correlations with piperazine (-.22). Correlations between Davis and Held et al. formulas and demographic variables including age, sex, race, education, age of onset, number of hospitalizations, and length of current hospitalization did not reveal significant relationship existence between CPZE levels and LNNB summary scale scores. No differences in these patterns were noted when subjects were grouped according to low and high CPZE levels (using mean CPZE as a cut off for groups) and grouped to low and high LNNB scores (using mean LNNB score as a cut off).

DISCUSSION

Traditionally, description of neuroleptic drug regimen has been limited to dosage and the relationship to dose and response is generally implied. In the present study, the investigators found that neuroleptic dose does not appear to be related to neuroleptic blood serum level and/or LNNB summary scale scores when three traditionally used dose conversion formulas and standard LNNB measures were employed. A fourth formula was highly correlated to neuroleptic blood serum levels but not to LNNB summary scale scores. Furthermore, it appears that specific drugs were differentially related to neuroleptic serum levels (correlations from -.22 to +.76). Interestingly, the highest correlations between dose and blood serum level were found for drugs administered with lithium. However, no relationships between neuroleptic blood serum level and neuropsychological performance as measured by the LNNB were found. Due to the number of analyses completed, the .01 level of significance was adopted thus further masking what may have been critical trends in this relationship.

From the present study, it appears that the use of a larger subject pool, an appropriate control group, other neuropsychological measures (especially those involving executive functions), fewer correlations, and restrictions of the type of conversion formulas might be beneficial for replication. In addition, the manipulation of drug levels may provide a clearer understanding of the effects of neuroleptics on neuropsychological performance. Finally, these studies were completed with chronic subjects who could have confounded the study because of a possible accumulation of neuroleptic drugs. Therefore, replication and extension of the present study with naive, acute subjects compared to an appropriate control group would be of interest.

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