EFFECTS OF VALPROMIDE ON ALERTNESS AND PSYCHOMOTOR SKILLS
DOUBLE BLIND AND CROSS-OVER STUDY VERSUS PLACEBO

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SUMMARY

The authors experiment Valpromide* on a population of 29 healthy volunteers to study the eventual side effects on alertness and psychomotor skills with a complete test battery including classic psychometric tests, computerized tests and a real car driving test.

Different pharmacological studies realised with primary Amine of Valproc acid, VALPROMIDE* do not show sedative potentiality relative to doses with which are usually observed anticonvulsives, antiagressives and anxiolytics effects of this molecule.

Administred to subjects considered as normal as to psychomotor activity, Valpromide doesn't seem to induce neither motodrowsiness, nor intellectual deterioration.

However, studies about the influence of Valpromide on vigilance are rather old, and it seems to be interesting to complete knowledge with a modern methodology already used for the evaluation of the secondary effects of psychotropic drugs.

Moreover, with respect to present day therapeutic indications of Valpromide in usual behaviour troubles as they are generally treated by general practitioners, many car drivers (or any engine drivers) are bound to drive while under treatment.

The incidence of the intake of Valpromide is difficult to access in a whole way.

The aim of this study is to experiment on an homogeneous population of healthy volunteers and to research influence on alertness and psychomotor skills versus placebo.

The monocentred was achieved in a double blind versus placebo, and cross over way on a population of 29 males, 19 to 42 years old, without any evolutive pathology and refraining from alcohol or drug consumption during the trial.

*DEPAMIDE, SANOFI-LABAZ, FRANCE

- Batman test: this test explores the subject in his way of recognizing lateral position of an image (left hand, right hand) presented 4 seconds in any position (20 trials).

Besides these laboratory tests, a real situation is explored with a driving test on a closed circuit.
The trial requires virtuosity with onwards and backwards slalom, hillstrait, passing precisely between pools.

This test is performed in a given time, without velocity criterium. The errors are added as ten seconds penalties to the given time or to the real time if this one is longer.

The test sequence is the same for all subjects and is preceded of a brief clinical examination, and of a recording of eventual side effects. A blood level of Valproate was measured at D7 and D21 (immuno enzymatic method, Abbot reactive).

This protocol was submitted to the ethical committee and the pharmaco vigilance commitee of Grenoble with acceptation.

Informed and written assent of subject was obtained before the trials. Products was administrated as pills dosed with 300 mg of Valpromide or 0 mg (placebo).

The administrated dose was 300 mg three times every day (900 mg day). Last pills was given at 08.00 A. M. on the day of passation. 29 subjects have entered the study and all of them have finished it.

RESULTS :

A statistical analysis was performed. The influence of Valpromide never reaches a significant level of P: 0,05.

A limit effect is noted for internal tension (P: 0,14) and numbers test (P: 0,08).

A period effect is noted for internal tension (P: 0,03), anxiety level (P: 0,05), numbers test (P: 0,02), Batman test (P: 0,04) and driving test (P: 0,05).

A treatment-period interaction is never noted.

This study concludes in the absence of statistically significant effects of Valpromide on alertness and psychomotor skills on those 29 subjects. Beyond simple statistical analysis, an analysis on every subject is realised to find an normal sensibility of a subject to Valpromide. By analysing every variation in test results for a given subject, it was not found homogeneous modifications for all the tests except an order effect already noted and usual in this sort of study.

The only data, no nignificant on a statistical way, let suppose the apparition of a subjective sensation of drowsiness or sleepyness, without modification of objective performances on therapeutic level as they were given. Those results are in correlation with precedent studies. Valpromide seems to be possible to give on those therapeutic level to car drivers by respecting usual conditions: to avoid association with psychotropical drugs intake or simultaneous alcohol consumption.
The assessments were performed:

- at D0 before any drug intake,
- at D7 after five days treatment (Valpromide or placebo),
- at D14 after nine days of wash out period,
- at D21 after five days treatment (placebo or Valpromide).

The test battery used each time lasted about 30 minutes, long enough to exhaust the reserve capacity, and short enough to keep the motivation (2.3.5.).

The test battery included:

- a self appraisal questionnaire about nervous tension, anxiety level, sleepyness, psychological drowsiness and physical diminution.

- a Zazzo's crossing out test (to study the velocity of performance in a simple intellectual operation consisting in crossing out or surrounding certain numbers on a list).

- a visual retention test (to study the capacity of visual retention and restitution of a simple image seen for five seconds).

- a tremometric test to study the voluntary control on muscle tone (two trials of one minute each separated by one minute rest period).

- three computerized tests whose interest results of strict standardisation of orders, but also in the possibility of evaluating not only results and time of passation, but also strategy of the subject, tracking in this way infraclinical deteriorations.

Those tests were performed on an APPLE II GS Computer.

- Numbers test: the subject has to classify by growing order, without possibility of correction, ten series of ten figures successivly presented.
- Squares test (computerared Zazzo's test): the subject has to recognize the images presented and to compare them with two reference images (100 images).


