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14. ABSTRACT
Forty-eight alcoholic patients, twelve psychiatric patients and thirteen healthy subjects were examined by the Cerberus system (measuring by rheoencephalogram-REG). REQ anacrotic time above 180 ms was considered pathological. Four groups were formed according to smoking habits and average daily alcohol dose. REQ anacrotic time was longer for the female patients ($p<0.01$). Comparison of alcoholic and drug patients showed significant short REQ anacrotic time for drug patients. Pathological REG value was found in twelve cases (9 alcoholics, 1 drug patient, 1 manic, I recurrent depressive). ANOVA showed: daily alcohol consumption and smoking were significantly higher in alcoholics than in drug patients or patients with depression. Factor analysis of variables showed gender differences. Three factors were found both for males (cumulative%64.86) and females (75.56). Factor I - age and REG anacrotic time (males) and age with vegetative indexes (females); Factor 2 - daily alcohol and cigarette consumption for both genders; Factor 3 - REG and vegetative index (males). Full abstract see in publication.

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CEREBROVASCULAR ALTERATIONS IN ALCOHOLIC AND NON-ALCOHOLIC PSYCHIATRIC PATIENTS

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Abstract

Forty-eight alcoholic patients, twelve psychiatric patients and thirteen healthy subjects were examined by the Cerberus system (measuring by rheoencephalogram-REG). REG anacrotic time above 180 ms was considered pathological. Four groups were formed according to smoking habits and average daily alcohol dose. REG anacrotic time was longer for the female patients ($p<0.01$). Comparison of alcoholic and drug patients showed significant short REG anacrotic time for drug patients. Pathological REG value was found in twelve cases (9 alcoholics, 1 drug patient, 1 manic, 1 recurrent depressive). ANOVA showed: daily alcohol consumption and smoking were significantly higher in alcoholics than in drug patients or patients with depression. Factor analysis of variables showed gender differences. Three factors were found both for males (cumulative%=64.86) and females (75.56). Factor 1 - age and REG anacrotic time (males) and age with vegetative indexes (females); Factor 2 - daily alcohol and cigarette consumption for both genders; Factor 3 - REG and vegetative index (males). Longer REG anacrotic time was correlated with higher daily alcohol consumption ($r=0.683$, $p=0.007$) in a subgroup ($n=12$). The US vs. Hungarian group comparison confirmed the cerebrovascular alteration in Hungarian alcoholic group. Elevated REG values in alcoholics may result from alcohol abuse and can be interpreted as accelerated arteriosclerosis.

Keywords: alcohol abuse, vascular aging, rheoencephalogram (REG).

Introduction

For most people who drink, alcohol is a pleasant accompaniment to social activities. Moderate alcohol use – for most adults, two drinks per day for men and one drink per day for women and older people, is not considered harmful. However, uncontrolled alcohol consumption causes mental and somatic disease.[1] Here we present initial results of a correlative study on alcoholic patients, using the Cerberus system, a computer-based screening system designed for primary prevention of cardiovascular disease, with emphasis on stroke (*Bodo, M., Thuroczy, G., Nagy, I., Peredi, J., Sipos, K., Harcos, P., Nagy, Z., Voros, J., Zoltai, L.* and *Oszvald, L.*, 1995). In the

[1]Anonymous, The National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD. http://www.niaaa.nih.gov/publications/booklet.htm

present study, Cerberus was applied to quantify the impact of alcohol on brain arteries. Measurement of psychological and somatic variables was performed to establish possible correlations with cerebrovascular alterations due to alcoholism. The study was carried out in a Psychiatric Unit (Kecskemét, Hungary) where patients with major psychiatric diagnoses, drug patients, and patients with alcohol abuse problems were examined. Additionally, a control group in the United States was measured.

Methods

Cerberus involves the measurement of pulsatile electrical impedance in the brain (Rheoencephalogram-REG), detailed elsewhere (*Bodo* et al., 1995; *Kornhauser*, 1987).[2] A/D sampling rate was 275 Hz. A one-minute REG recording was used for signal averaging, triggered by the EKG R wave. The left and right side REG data were averaged for each person. REG anacrotic time was measured and evaluated as a symptom of cerebrovascular alteration (*Jenkner*, 1986). For the measurement of IQ, the Hungarian version (MAWI) of Wechsler Adult Intelligence Scale[3]; for anxiety measurement, the short form of STAI (*Hanin* and *Spielberger*, 1983) was used twice for each subject. ANOVA (SAS) and student t-test in Excel (Microsoft, Redmond, WA) was used for statistical evaluation. $P < 0.05$ was considered significant.

Subjects

1) Kecskemét (K) sample: Three groups were compared (drug abuse, alcohol abuse, depression). The alcohol abuse patients were middle-aged inpatients identified as having alcohol problems for more than ten years (N=44, mean age: 41 y), who were participating either in detoxification (Diagnosis[4]: F10.30, F10.40) or abstinence treatment programs (Dg: F10.10, F10.20, F10.80). Their age varied from 27 to 54 years for males and from 27 to 56 years for females. The drug abuse patients contained 2 subjects with dependency (F12.20, F13.20), and 4 subjects with a diagnosis of abusive disorders (F11.10, F18.10, F19.10) (N=6, mean age: 31 y). The two female drug patients' ages were 25 and 31 y. The depressive subjects (N=6, mean age: 51 y) (F32.00, F32.20, F333.20) were non-psychotic. In the drug patient group, the youngest and oldest subjects were males (19 and 49 years of age). The male/female ratio for alcoholic patients (32:12), for drug patients (4:2), and for depressive patients (1:5) mirrored the general tendency of the gender distribution for these mental disorders. Blood pressure, body mass index (BMI) and modified (by Sipos) vegetative balance by Kerdo were measured and calculated. Kerdo index and anxiety was used twice for each subject.

2) USA sample (Silver Spring -SS): 13 healthy male subjects were tested as a control group for REG comparison with the (K) (alcoholic) sample only. Both REG samples also were analyzed dividing young (below 40 y) and old (above 40 y) subgroups.

[2] Bodo, M., Nagy, I., Peredi, J., Thuroczy, G. and Ozsvald, L., inventors; Process and equipment for diagnosing circulation (cerebrovascular) disorders. *Hungarian patent P 92 01 1079.* 1992 Mar 31; *International patent PCT/HU 93/00006*; PCT Pub. No: WO 93/19665. *US patent 5,584,297.* 1996 Dec 17.

[3] *Wechsler Adult Intelligence Scale—Revised,* http://www.cps.nova.edu/~cpphelp/WAIS-R.html

[4] The ICD-10 International Statistical Classification of Diseases and Related Health Problems (10th Revision) WHO Geneva, Switzerland, 1992. http://www.who.int/msa/mnh/ems/icd10/icd10.htm

Results

The most important result of this study was that the longer REG anacrotic time was parallel to the higher quantity of daily alcohol consumption in the MAWI subgroup (n=12). BMI and MAWI dementia % showed a statistically significant positive correlation (r=0.599; p=0.020) in the same subgroup. The daily alcohol consumption correlated to REG anacrotic time (r=0.683; p=0.007); dementia % vs. BMI (r=0.599, p=0.020) was used twice for each subject vs. risk factors (r=0.610, p=0.018), anxiety-2 vs. risk factors (r=0.538, p=0.036).

Alcoholic-drug-depression groups: Significant differences were found for age between the drug (31.33 ± 11.88 y) and depression (47.75 ± 10.36 y, p=0.017) groups and for the alcohol (42.44 ± 7.72 y) and drug groups (p=0.003). The REG anacrotic time was significantly different for the drug (79.75 ± 59.05 ms) and alcohol (108.38 ± 61.85 ms) groups (p=0.025). The systolic arterial pressure, BMI, Kerdo index values showed no significant differences among the three groups.

Healthy vs. alcoholic groups: The age difference of REG anacrotic time in the K male and female alcoholics was not significant; therefore, males and females were placed in a single group. In young subjects tested, no significant differences in REG and age were observed for Hungarians and US subjects. Between older groups, significant differences both in age and in REG anacrotic time were observed (Table 1). The REG anacrotic time in the K alcoholic group had a dual peak distribution – around a lower mean anacrotic time (99.43 ± 56.56, n=33) and a higher one (133 ms ± 71.39, n=12). Between these groups the significant difference was the REG time (p< 0.0001) and the systolic arterial pressure (p=0.0159). The Kerdo vegetative index, diastolic arterial pressure, heart rate, TIA symptoms, incidence of stroke risk factors, level of anxiety, BMI, and age difference were not significant. For further comparisons, see Figure 1, 2, and 3.

Table 1: Numeric characteristics of Hungarian (K) and US (SS) REG groups

	K young		SS young		K old		SS old	
	Age (year)	REG (ms)	Age (year)	REG (ms)	Age (year)	REG (ms)	Age (year)	REG (ms)
Mean	24.00	64.35	22.33	65.50	43.88	111.28	47.57	60.71
SD	4.04	13.73	4.37	8.34	2.92	61.32	4.58	5.65
Count	7	7	6	6	34	34	7	7
P							0.009*	0.037*

* P value of a t-test between Hungarian old (K) and US old (SS) groups.

Sorted age and REG in Hungarian alcoholic group. After sorting independently the REG anacrotic time and age these variables show the presented distribution. The age regression was: y = 0.5697x + 29.341,

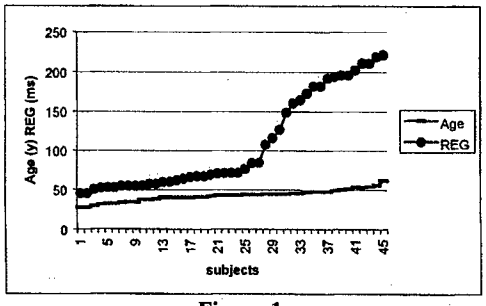

Figure 1.

$R^2 = 0.9398$ (linear). The REG regression was: $y = 4.3882x + 7.4492$, $R^2 = 0.8682$ (linear) and $y = 36.685e^{0.0404x}$, $R^2 = 0.9279$ (exponential).

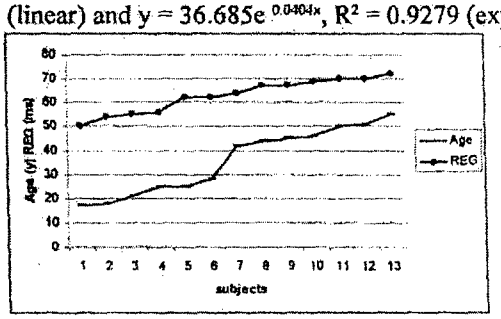

Figure 2.

Sorted age and REG in US healthy group. US age and REG regression data (calculated as one group, n=13) are as follow: Age: $y = 3.4505x + 11.769$, $R^2 = 0.9509$, and REG: $1.7912x + 50.385$, $R^2 = 0.9527$ (both linear).

Relationship of age and REG anacrotic time in Hungarian alcoholic group, sorted by REG value: <100 ms (27 subjects) or > 140 ms (15 subjects). The <100 ms subgroup mean age was: 40.37 ± 8.16 y. The > 140 ms mean age was 44.93 ± 5.89 y. The difference was not significant (p=0.0641). The <100 ms subgroup mean REG was: 62.00 ± 10.54 ms. The > 140 ms mean REG was 190.19 ± 21.71 ms. The difference was significant (p<0.00001). Such comparison was not applicable in the US group.

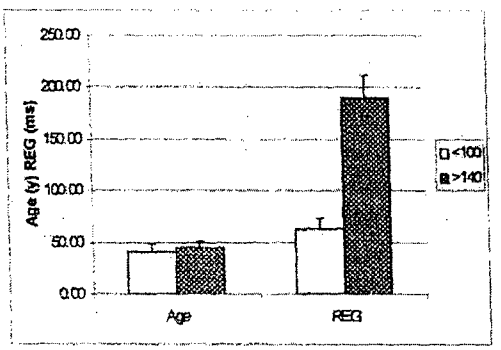

Figure 3.

Discussion

Light-to-moderate alcohol consumption seemed to decrease the risk of ischemic stroke by reducing atherothrombotic events, but the underlying mechanism is still unclear; heavy drinking increased the risk for both hemorrhagic and ischemic strokes (*Hillbom*,1998). It is known that the nervous system is particularly susceptible to the harmful effects of alcohol, which can affect both neuronal tissue and the cerebral arteries (*Lofti* and *Meyer*, 1989).

In this study we used various methods to measure the effects of regular alcohol consumption on the nervous system, including vascular, psychological and cognitive deterioration as well as somatic co-morbidity (prevalence of arteriosclerosis risk factors).

A difference was observed between the Hungarian alcoholic group and the drug/depression groups; a difference was also observed between healthy older US subjects and older alcoholic Hungarian subjects. The fact that cardiovascular risk and stroke mortality in Hungary is higher than in the USA does not account for this result (*Bodo* et al., 1995; *Bonita* and *Stewart*, 1990; *Bodo*, *Thuroczy*, *Brockbank* and *Sipos*, 1998; *Sipos*, *Bodó*, *Veér* and *Hagtvet*, 1993). REG anacrotic time above 180 ms was considered pathological (*Jenkner*, 1986). In our study, 11 subjects in the Hungarian alcoholic group surpassed this level.

For all healthy subjects, physiological cerebrovascular aging was expected to show an identical slope with age. In the Hungarian alcoholic group, the sharper REG slope: 36.68 vs. age: 0.56 (ratio: 64.39) reflects the pathological impact of alcohol abuse. The US control sample showed a nearly identical slope for both REG (1.79) and age (3.45; ratio: 0.52). The correlation of increased REG and daily alcohol consumption quantitatively supports the hypothesis of accelerated cerebrovascular aging of the alcoholic subjects.

Future studies may involve comparison of REG to EEG measurements in order to reveal the direct neuronal and vascular effect of alcohol abuse on cerebral arteries in the same subjects. Such studies would be a significant step toward realizing the objectives of evidence-based medicine. REG shows potential to support neurological differential diagnosis with a practical new tool.

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References

Bodo, M., Thuroczy, G., Nagy, I., Peredi, J., Sipos, K., Harcos, P., Nagy, Z., Voros, J., Zoltai, L. and Ozsvald, L. (1995): A complex cerebrovascular screening system (Cerberus). *Medical Progress through Technology*, 21(2).53-66.

Kornhauser, S.H. (1997): Cerebrovascular diagnostic system. *American Journal of Electromedicine*, June. 69-71.

Jenkner, F.L. (1986): *Clinical rheoencephalography*. Ertldruck, Vienna.

Hanin, Y.L. and Spielberger, C.D. (1983): *The development and validation of the Russian Form of the State-Trait Anxiety Inventory.* In: Spielberger, C.D. and Diaz-Guerrero, R. (Eds.): Cross-cultural Anxiety. Vol.2, Washington: Hemisphere Publishing Corporation. 15-26.

Hillbom, M. (1998): Alcohol consumption and stroke: benefits and risks. *Alcohol Clin Exp Res.*, 22 (7. Suppl.):352-358.

Lotfi, J. and Meyer, J.S. (1989): Cerebral hemodynamic and metabolic effects of chronic alcoholism. *Cerebrovasc. Brain Metab. Rev.*, 1(1).2-25.

Bonita, R. and Stewart, A. (1990): Beaglehole R. International trends in stroke mortality: 1970-1985. *Stroke*, 21.989-992.

Bodo, M., Thuroczy, Gy., Brockbank, K.G.M. and Sipos, K. (1998): *Cerebrovascular aging assessment by Cerberus.* In: Klatz, R.M. and Goldman, R. (Eds.): Anti-Aging Medical Therapeutics. Vol. II Health Quest Publications, Marina Del Ray, WA. 86-95.

Sipos, K., Bodó, M., Veér, A. and Hagtvet, K.A. (1983): *Neurosis, depression, anxiety and stroke risk factors in a Hungarian village.* VIIth European Health Psychology Society Conference. Brussels, 1–3 September, Abstracts, 90. and *Kalokagathia* XXXII. 1: 1994. 1. 94–114.