Copper and Zinc Levels in Hair of Schizophrenics and Depression Patients

Abd Elaziz A., Essam M., Amal A., Doaa A., Sherif M., El Sayed S. and Hanan E.

Faculty of Medicine, Mansoura University, Egypt.

Date received: 8/4/2008
Date accepted: 4/9/2008

Background: Copper stimulates the diencephalons or old brain and its overall effect appears to enhance all emotional states in a human being. While, Zinc is needed for the new brain or cortex. This brain is associated with the "higher emotions" such as reasoning, compassion and love.
Objectives: The aim of this paper is to estimate hair copper and zinc levels in schizophrenic and depressive patients and to correlate these levels to the severity of schizophrenia and major depressive disorder.
Subjects & Methods: The study was carried on 80 persons (male and female), with their age between 20 – 40 years; 20 of them (10 males and 10 females) were healthy control, 30 (15 males and 15 females) were suffering from schizophrenia (group I) and 30 (15 males and 15 females) were suffering from major depressive disorder (group II). Exclusion criteria for all persons selected for the study included another comorbid psychiatric disorder, pregnancy, and medical disorders (endocrine, liver cirrhosis, renal) or drugs (anticonvulsants, contraceptives, glucocorticoids) known to affect trace element metabolism. Approximately 100 mg of scalp hair samples were cut from each person as close to the scalp as possible. Zinc and copper levels in hair samples were determined by atomic absorption spectrophotometry after wet ashing.
Results: The mean hair copper level was significantly higher in both schizophrenic patients (group I) and depression patients (group II) when compared with its mean levels in healthy control group. The mean hair zinc level was significantly lower in both schizophrenic patients (group I) and depression patients (group II) when compared with its mean levels in healthy control group. In depression patients the mean hair copper level was insignificantly higher meanwhile, the mean hair zinc level was significantly lower when compared with their mean level in schizophrenic patients.
Conclusion: From these results, it can be concluded that copper intoxication and zinc deficiency may have a role in pathogenesis of both schizophrenia and depression disorders. It can also be concluded that zinc deficiency has more important role in inducing depressive disorders. So, it is recommended to evaluate both copper and zinc hair and serum levels in schizophrenic and depressive patients especially in patients resistant to therapy as this may have a prognostic value. It is recommended also to use zinc supplementation during antidepressant therapy as it may improve response to therapy and/ or decrease the dose that can minimize the side effects of antidepressants.

Keywords: Copper, Zinc, Major depressive disorders, Schizophrenia.

Abbreviations:
Cu: Copper
Zn: Zinc
DSM IV TR: Diagnostic and Statistical Manual of mental disorders (4th division Text Revised)
PANSS: Positive and negative syndrome scale

Egypt. J. Psychiatry, Jan 2010; 30(1): 23-30

INTRODUCTION

Copper and zinc, two essential trace elements, have been studied in many diseases, including autoimmune, neurologic and psychiatric disorders (Cramer, 1983). Copper is called the "Emotional mineral". The reason for this is that copper and imbalances related to it have such a profound impact on the central nervous system. The psychiatric implications of copper imbalance are tremendous, even if copper did not affect other body systems. The overall effect of copper appears to be to enhance all emotional states in a human being. It is felt that copper stimulates the diencephalons or old brain. Zinc is needed for the new brain or cortex. This brain is associated with the "Higher emotions" such as reasoning, compassion and love. When an imbalance between these exists, the person tends to revert to the use of the old brain, also called the animal brain or emotional brain. This can lead to a tendency for every possible emotional condition affecting human beings (Eck and Wilson 1989).

Copper is a component of several metalloenzymes linked to dopamine synthesis, in biochemical pathways involving either antagonism of dopamine production or catalysis of its breakdown. As dopamine is implicated in schizophrenia, copper homeostasis may be particularly relevant: an excess of copper may be associated with dopamine dys-regulation (Bowman and Lewis, 1982). Zinc is required for the structural integrity and/

or catalysis of more than 200 enzymes, the majority of which are zinc metalloenzymes involved in nucleic acid and protein synthesis (Abdel Mageed and Oehme, 1990). Whenever zinc becomes deficient, copper tends to accumulate (Yanik, et al. 2004).

The findings of previous research on the status of trace elements in patients with schizophrenia have been controversial (Herran, et al. 2000). Some authors did not find significant deviation from normal in concentrations of copper in serum (Gillin, et al. 1982) or found a decrease in hair copper concentrations in female chronic schizophrenics (Suzuki, et al. 1992). Others demonstrated significant increase in the serum and hair concentration of Cu and significant decrease in Zn in schizophrenic patients than that of their levels in control group (Tokdemir, et al. 2003; Wolf, et al. 2006 and Rahman, et al. 2009).

It was found also that major depressed subjects had significantly lower serum zinc concentrations than normal controls and that clinical improvement was accompanied by increments in serum zinc (McLoughlin and Hodge, 1990). Meanwhile, copper levels and Cu/Zn ratios were significantly higher in women having a history of post-partum depression (Crayton and Walsh, 2007).

This study was undertaken to estimate hair copper and zinc levels in schizophrenic patients and patients with depression and whether these levels could be correlated to the severity of schizophrenic and depression illness.

SUBJECTS AND METHODS

Subjects:

The study was carried on 80 male and female persons; 20 of them (10 males and 10 females) were healthy control, 30 (15 males and 15 females) were suffering from schizophrenia (Group I) and 30 (15 males and 15 females) were suffering from major depression (Group II). The age of all persons of the study is between 20–40 years with mean age 30.1±5.572 in control group, 30.267±5.632 in group I and 30.633±5.543 in group II. Exclusion criteria for all persons selected for the study included another comorbid psychiatric disorder, pregnancy, and medical disorders (Endocrine, liver cirrhosis, renal) or drugs (Anticonvulsants, contraceptives, glucocorticoids) known to affect trace element metabolism. These criteria were determined according to study of Farzin, et al. (2006). The exclusion is done through history taking and routine laboratory investigations.

Patients were recruited from psychiatry department of Mansoura University Hospital. Assessment and diagnosis of schizophrenic & depressive patients were made according to the Diagnostic and Statistical Manual of mental disorders (4th division Text Revised) DSM IV TR criteria. Positive and negative syndrome scale (PANSS) for schizophrenia which was developed and standardized by Kay, et al. (1987) was used as adjunct to the positive-negative symptoms assessment to provide a parallel measure of severity of schizophrenic illness. The score based on General Psychopathology Scale (Ranged from 16-112) was used for testing of statistical correlation between severity of schizophrenic illness and zinc and copper level in hair. Assessment the severity of depression was made according to translated self-report rating inventory which was developed by Beck, et al. (1961) that measure characteristic attitudes and symptoms of depression and its severity.

Samples collection:

Approximately 100mg of scalp hair samples were cut from each person with stainless-steel scissors in the nape or occipital regions, as close to the scalp as possible. Hair collection was carried out in dust-free environment and hair treated with artificial color was excluded from the study. The distal ends of the hair were cut from the samples. Each hair sample was comminuted, washed consecutively in neutral detergent, ether and acetone and dried before analyses according to the procedure originally described by Sorenson, et al. (1973).

Biochemical studies:

Zinc and copper levels in hair samples were determined by atomic absorption spectrophotometry after wet ashing using reagent-grade HNO3 and HClO4 according to Eads and Lambdin, (1973). For analyses the Model Varian Spectra AA–400 atomic absorption spectrophotometer was used. Atomization signals were recorded from the digital readout. The light sources were zinc and copper hollow-cathode lamps. Uncoated graphite tubes (Varian 63–100015–00) were used for furnace. Wavelengths were set at 324.8 and 213.9nm for copper and zinc respectively.

Statistical analysis:

Statistical analysis was done by using the Statistical Package for Social Science (SPSS) program version 12. The following statistical parameters were utilized: arithmetic mean (x), standard deviation (± SD), Student t-test and correlation coefficient. Significance was considered at P value less than 0.05.

RESULTS

The mean hair copper levels were 29.8ug/mg ± 5.460 in control group, 46.823ug/mg ± 9.660 in schizophrenic patients (Group I) and 48.597ug/mg ± 15.751 in depressive patients (Group II). The mean hair zinc levels were 488.225ug/mg ± 6.564 in control group,

421.08ug/mg ± 54.696 in schizophrenic patients (Group I) and 381.47ug/mg ± 70.745 in depressive patients (Group II) (Table 1).

The mean hair copper level was significantly higher in both schizophrenic patients (Group I) and depressive patients (Group II) when compared with its mean levels in healthy control group. In depressive patients the mean hair copper level was insignificantly higher when compared with its mean level in schizophrenic patients (Table 1 and Figure 1).

The mean hair zinc level was significantly lower in both schizophrenic patients (Group I) and depressive patients (Group II) when compared with its mean levels in healthy control group. In depressive patients the mean hair zinc level was significantly lower when compared with its mean level in schizophrenic patients (Table 1 and Figure 2).

Table 1: Comparison between mean hair copper and zinc levels (ug/mg) in all groups of the study:

Parameters \ Groups		Control Group	Group (I)	Group (II)
Hair copper level (ug/mg)	Mean±SD	29.8±5.460	46.823±9.660	48.597±15.751
	P_1		↑ < 0.001*	↑ < 0.001*
	P_2			↑ 0.638
Hair zinc level (ug/mg)	Mean±SD	488.225±6.564	421.08±54.696	381.47±70.745
	P_1		↓ < 0.001*	↓ < 0.001*
	P_2			↓ < 0.05*

***=** Significant if P<0.05 Insignificant if P>0.05

↑**=** higher ↓**=** lower

Group I: Schizophrenic patients. **Group II:** Depressive patients.

P_1: Schizophrenics and depressive patients versus control.

P_2: Depressive patients versus Schizophrenics patients.

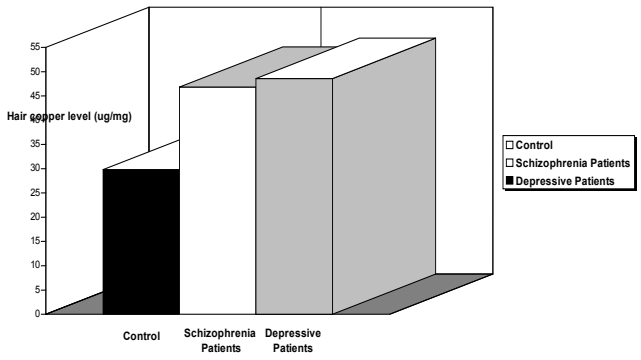

Fig.1: Mean hair copper level (ug/mg) in control and patients groups.

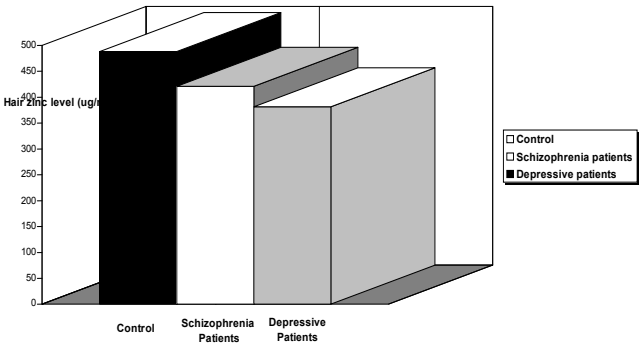

Fig. 2: Mean hair zinc level (ug/mg) in control and patients groups.

Results of the present study showed significant positive correlation between hair copper level and the severity of illness in schizophrenics and depressive patients. On the other hand, significant negative correlation was found between hair zinc level and the severity of illness in the same cases (Table 2 and Figures 3-6).

Table 2: Correlation between hair copper and zinc levels and schizophrenia general psychopathology score and depression score:

		Hair copper level	Hair zinc Level
Schizophrenia general psychopathology score	Pearson correlation	0.984**	-0.943**
	Sig. (2-tailed)	0.000	0.000
	N	30	30
Depression score	Pearson correlation	0.994**	-0.973**
	Sig. (2-tailed)	0.000	0.000
	N	30	30

**Correlation is significant at 0.01 level (2-tailed).

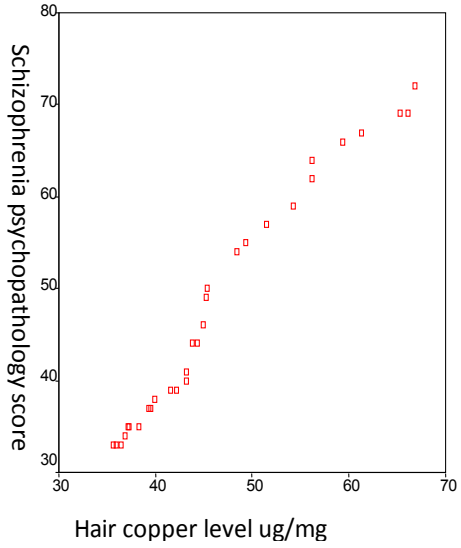

Fig. 3: The statistical correlation between hair copper level and severity of schizophrenic symptoms assessed by PANSS general psychopathology score:

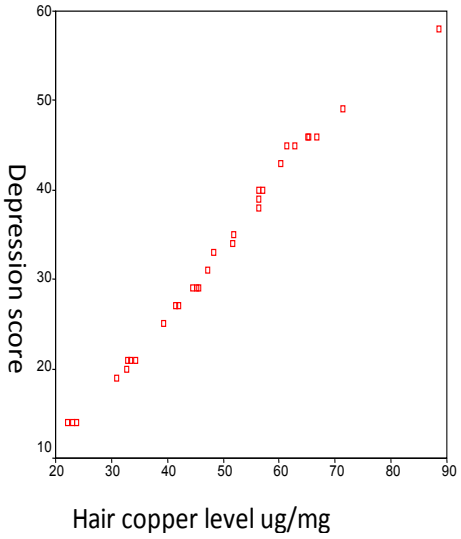

Fig. 5: The statistical correlation between hair copper level and Severity of depressive symptoms assessed by translated self-report rating inventory which was developed by Beck, et al. (1961).

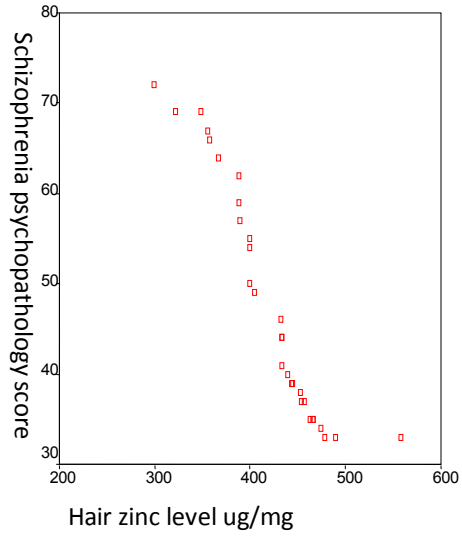

Fig. 4: The statistical correlation between hair zinc level and severity of schizophrenic symptoms assessed by PANSS general psychopathology score.

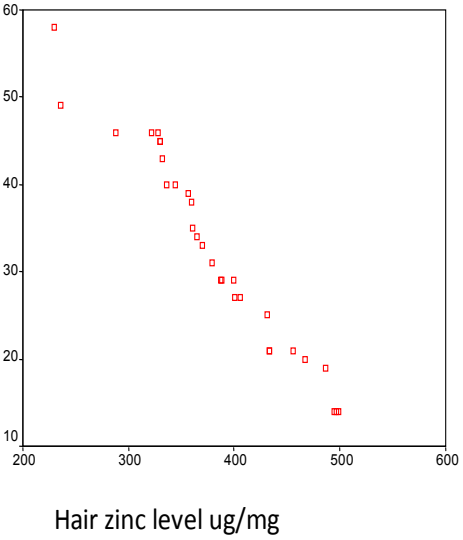

Fig. 6: The statistical correlation between hair copper level and Severity of depressive symptoms assessed by translated self-report rating inventory which was developed by Beck, et al. (1961).

DISCUSSION

Deficiency as well as excess in either zinc or copper can produce a variety of biochemical and physiologic changes (Ma and Betts, 2000). In addition, these two essential trace elements are neuroactive substances that can be synaptically released during neuronal activity. They have been implicated in diseases with neuropathological components (Strausak, et al. 2001).

Previous observations suggested that there may be an association between elevated serum and hair copper (Cu) levels and decreased serum and hair (Zn) levels and some psychiatric disorders. A relation between low concentrations of zinc and mental health problems, especially in at risk populations has been demonstrated. Zinc deficiency induced depression-like behavior in mice that was incompletely corrected by antidepressant therapy (Whittle, et al. 2009).

The results of the present work showed significant increase in the mean hair copper level and significant decrease in the mean hair zinc level in schizophrenic patients compared with their mean levels in healthy control group. Similar results were found in the study of Rahman, et al. (2009). Another earlier study found that serum copper and ceruloplasmin were elevated in schizophrenia (Wolf, et al. 2006). Nechifor, et al. (2004) observed also that Cu/Zn ratios were increased in patients with acute paranoid schizophrenia episode and in addition they found that Zn levels but not Cu in plasma was found to improve after 3 weeks of some antipsychotic treatment. In criminal schizophrenic subjects, Tokdemir, et al. (2003) found that serum copper values were significantly higher while zinc values were significantly lower than non-criminal subjects.

In disagreement of our results, the study of Gillin, et al. (1982), who found that patients with acute and chronic schizophrenia, on or off treatment with various major tranquillizers, did not show any significant deviation from normal in concentrations of zinc or copper in serum, urine, or gastric fluid, in serum ceruloplasmin or in hair zinc. Suzuki, et al. (1992) found also a decrease in hair copper concentrations in female chronic schizophrenics. This heterogeneity of the data may be attributed to heterogeneity of patients Nechifor, et al. (2004) or may be due to heterogeneity of schizophrenic pathologies.

The role of copper and ceruloplasmin in schizophrenia remains unclear. Although elevation of copper and ceruloplasmin may be an effect related to other factors and insufficient alone to infer pathogenic causality, it may be that copper abnormalities play a role in schizophrenia by exacerbating or perpetuating dopaminergic dysregulation. However it is unknown at this stage whether the copper contributes to the mental illness, whether the body attempts to store more copper in response to the illness, or whether the high levels of copper are the result of the mental illness. Others postulated that elevated Cu levels may be a consequence of antipsychotic treatment (Bowman and Lewis, 1982).

The results of the present work showed also significant increase in the mean hair copper level and significant decrease in the mean hair zinc level in depression patients compared with their mean levels in healthy control group. In addition, zinc levels were significantly lower in depression patients compared to schizophrenic patients. Similarly, Manser, et al. (1989) and Narang, et al. (1991) found that Cu levels were significantly higher in depressives than in the normal and after recovery from depression. Others found that major depressed subjects had significantly lower serum zinc concentrations than normal controls (McLoughlin and Hodge, 1990). Even lower serum Zn was considered a marker of treatment resistance and of the immune/ inflammatory response in depression (Maes, et al. 1997). Also, copper levels and Cu/Zn ratios were significantly higher in women having a history of post-partum depression (Crayton and Walsh, 2007).

Copper/zinc superoxide dismutase coenzyme concentrations in postmortem prefrontal cortical regions of the brain was significantly increased in patients with recurrent depressive disorder evidencing oxidative stress in the pathophysiology of depressive disorder (Michel, et al. 2007).

Contradictory to the previous results, Maes, et al. (1997) concluded that, there were no significant effects of antidepressive treatment on serum Zn, whereas serum Cu was significantly reduced.

The significant negative correlation that found in the present work between hair zinc level and the severity of both schizophrenic illness and depression support the study of Pfeiffer and Braverman, (1982) who stated that zinc has been employed with success to treat specific types of schizophrenia. These coincide also with McLoughlin and Hodge, (1990) who found that clinical improvement of major depressed subjects was accompanied by increments in serum zinc.

The clinical efficacy of current antidepressant therapies is unsatisfactory; antidepressants induce a variety of unwanted effects, and, moreover, their therapeutic mechanism is not clearly understood (Szewczyk, et al. 2008). Zinc and magnesium exhibit antidepressant like activity in a variety of tests and models in laboratory animals and the efficacy of pharmacotherapy is enhanced by supplementation with zinc and magnesium particularly in patients previously nonresponsive to antidepressant pharmacotherapies (Cunha, et al. 2008 and Siwek, et al. 2009).

From the results of the present work, it can be concluded that copper intoxication and zinc deficiency may have a role in pathogenesis of both schizophrenia and depression disorders. It can also be concluded that zinc deficiency has more important role in inducing depressive disorders.

It is recommended to evaluate both copper and zinc hair and serum levels in schizophrenic and depression patients especially in patients resistant to therapy as this may have a prognostic and therapeutic value. It is recommended also to use zinc supplementation during antidepressant therapy as it may improve response to therapy and/or decrease the dose that can minimize the side effects of antidepressants. In addition, frequent screening of psychiatric symptoms is recommended for individual chronically exposed to copper. Zinc reach food as meat is advised to minimize liability to develop depressive disorders.

Corresponding Author
Assistant Professor. El Sayed Saleh
Assisstant Professor of Psychiatry, Faculity of Medicine El Mansoura Univerisity
E-mail: elsayedsaleh@yahoo.com

REFERENCES

Abdel Mageed, A. B., and Oehme, F. W. 1990. A review of the biochemical roles, toxicity and interactions of zinc, copper and iron: I. Zinc. Veterinary and Human Toxicology 32(1):34-39.

Beck, A. T., Ward, C. H., Mendelson, M., et al. 1961. An inventory for measuring depression. Archives of General Psychiatry 4: 561-571.

Bowman, M. B., and Lewis, M. S. 1982. The copper hypothesis of schizophrenia: A review. Neuroscience and Biobehavioral Reviews 6(3):321-328.

Cramer, J. L. 1983. Trace elements in neuropsychiatry. British Journal of Psychiatry 143:85-88.

Crayton, J. W., and Walsh, W. J. 2007. Elevated serum copper levels in women with a history of post-partum depression. Journal of Trace Elements in Medicine and Biology 21(1):17-21.

Cunha, M. P., Machado, D. G., Bettio, L. E. B., et al. 2008. Interaction of zinc with antidepressants in the tail suspension test. Progress in Neuro-Psychopharmacology and Biological Psychiatry 32(8):1913-1920.

Eads, E. A., and Lambdin, C. E. 1973. A survey of trace metals in human hair. Environmental Research 6(3):247-252.

Eck, P. C., and Wilson, L. 1989. Toxic metals in human health and disease. Phoenix, AZ: Eck Institute of Applied Nutrition and Bioenergetics Ltd.

Farzin, D., Mansouri, N., and Yazdani, T. 2006. Elevated plasma copper/zinc ratios in patients with schizophrenia. European Neuropsychopharmacology 16(Suppl 4):S364-S365.

Gillin, J. C., Carpenter, W. T., Hambidge, K. M., et al. 1982. Zinc and copper in patients with schizophrenia. L'Encephale 8(3): 435-444.

Herran, A., Garcia Unzueta, M. T., Fernandez Gonzalez, M. D., et al. 2000. Higher levels of serum copper in schizophrenic patients treated with depot neuroleptics. Psychiatry Research 94(1):51-58.

Kay, S. R., Fiszbein, A., and Opler, L. A. 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bulletin 13(2):261-276.

Ma, J., and Betts, N. M. 2000. Zinc and copper intakes and their major food sources for older adults in the 1994-96 continuing survey of food intakes by individuals (CSFII). The Journal of Nutrition 130(11):2838-2843.

Maes, M., Vandoolaeghe, E., Neels, H., et al. 1997. Lower serum zinc in major depression is a sensitive marker of treatment resistance and of the immune/inflammatory response in that illness. Biological Psychiatry 42(5):349-358.

Manser, W. W., Khan, M. A., and Hasan, K. Z. 1989. Trace element studies on Karachi population. Part IV: Blood copper, zinc, magnesium and lead levels in psychiatric patients with depression, mental retardation and seizure disorders. JPMA. The Journal of the Pakistan Medical Association 39(10):269-274.

McLoughlin, I. J., and Hodge, J. S. 1990. Zinc in depressive disorder. Acta Psychiatrica Scandinavica 82(6):451-453.

Michel, T. M., Frangou, S., Thiemeyer, D., et al. 2007. Evidence for oxidative stress in the frontal cortex in patients with recurrent depressive disorder--a postmortem study. Psychiatry Research 151(1-2):145-150.

Narang, R. L., Gupta, K. R., Narang, A. P., and Singh, R. 1991. Levels of copper and zinc in depression. Indian Journal of Physiology and Pharmacology 35(4):272-274.

Nechifor, M., Vaideanu, C., Palamaru, I., et al. 2004. The influence of some antipsychotics on erythrocyte magnesium and plasma magnesium, calcium, copper and zinc in patients with paranoid schizophrenia. Journal of the American College of Nutrition 23(5):549S-551S.

Pfeiffer, C. C., and Braverman, E. R. 1982. Zinc, the brain and behavior. Biological Psychiatry 17(4):513-532.

Rahman, M. A., Azad, M. A. K., Hossain, M. I., et al. 2009. Zinc, manganese, calcium, copper and cadmium level in scalp hair samples of schizophrenic patients. Biological Trace Element Research 127(2):102-108.

Siwek, M., Dudek, D., Paul, I. A., et al. 2009. Zinc supplementation augments efficacy of imipramine in treatment resistant patients: A double blind, placebo-controlled study. Journal of Affective Disorders [Article in press].

Sorenson, J. R., Melby, E. G., Nord, P. J., and Petering, H. G. 1973. Interferences in the determination of metallic elements in human hair. An evaluation of zinc, copper, lead and cadmium, using atomic absorption spectrophotometry. Archives of Environmental Health 27(1):36-39.

Strausak, D., Mercer, J. F., Dieter, H. H., et al. 2001. Copper in disorders with neurological symptoms: Alzheimer's, Menkes and Wilson diseases. Brain Research Bulletin 55(2):175-185.

Suzuki, T., Koizumi, J., Moroji, T., et al. 1992. Effects of long-term anticonvulsant therapy on copper, zinc and magnesium in hair and serum of epileptics. Biological Psychiatry 31(6):571-581.

Szewczyk, B., Poleszak, E., Sowa-Kućna, M., et al. 2008. Antidepressant activity of zinc and magnesium in view of the current hypotheses of antidepressant action. Pharmacological Reports 60(5):588-599.

Tokdemir, M., Polat, S. A., Acik, Y., et al. 2003. Blood zinc and copper concentrations in criminal and noncriminal schizophrenic men. Archives of Andrology 49(5):365-368.

Whittle, N., Lubec, G., and Singewald, N. 2009. Zinc deficiency induces enhanced depression-like behaviour and altered limbic activation reversed by antidepressant treatment in mice. Amino Acids 36(1):147-158.

Wolf, T. L., Kotun, J., and Meador Woodruff, J. H. 2006. Plasma copper, iron, ceruloplasmin and ferroxidase activity in schizophrenia. Schizophrenia Research 86(1-3):167-171.

Yanik, M., Kocyigit, A., Tutkun, H., et al. 2004. Plasma manganese, selenium, zinc, copper and iron concentrations in patients with schizophrenia. Biological Trace Element Research 98(2):109-117.

الملخص العربى

مستويات النحاس والزنك فى شعر مرضى الفصام والإكتئاب الجسيم

عبد العزيز أبو الفتوح غانم، عصام ممدوح على، أمال عبد السلام البقرى، دعاء عبد الوهاب، شريف محمد القنيشى، السيد صالح حسين وحنان السيد
قسم الطب الشرعى والسموم الإكلينيكية وقسم الأمراض النفسية
(كلية الطب–جامعة المنصورة)

أجريت هذه الدراسة على ٨٠ شخصاً من الذكور والإناث تتراوح أعمارهم بين ٢٠ و٤٠ عاماً، ٢٠ منهم أشخاص أصحاء وإعتبروا كمجموعة ضابطة (١٠ من الذكور و١٠ من الإناث)، ٣٠ منهم كانوا يعانوا من مرض الفصام (١٥ من الذكور و١٥ من الإناث) وإعتبروا المجموعة الأولى، ٣٠ آخرون كانوا يعانوا من مرض الإكتئاب الجسيم (١٥ من الذكور و١٥ من الإناث) وإعتبروا المجموعة الثانية. عند إختيار الأشخاص التى أجريت عليهم الدراسة تم إستثناء الأشخاص المعرضون لأحوال تؤثر على أيض العناصر الضئيلة مثل الحمل والإضطرابات الطبية والنفسية الأخرى وبعض الأدوية. تم قص حوالى ١٠٠ مجم من شعر فروة الرأس وتم تحديد مستويات النحاس والزنك فى عينات الشعر بالإمتصاص الذرى بجهاز مقياس الطيف الضوئى. ووجد أن متوسط مستوى النحاس مرتفعاً بقيمة ذات دلالة إحصائية ومتوسط مستوى الزنك منخفضاً بقيمة ذات دلالة إحصائية فى عينات شعر كل من مرضى الفصام والإكتئاب عنه فى عينات شعر الأشخاص الأصحاء، كما وجد فى عينات شعر مرضى الإكتئاب أن متوسط مستوى النحاس كان أكثر إرتفاعاً بقيمة ليست ذات دلالة إحصائية ومتوسط مستوى الزنك كان أكثر إنخفاضاً بقيمة ذات دلالة إحصائية عند مقارنتهم بمتوسط مستويات النحاس والزنك فى شعر مرضى الفصام.