Breath Analysis of Hepatic Patients Using Electronic Nose

Özgür Örnek

International Burch University, Department of Information Technology

E-mail: *oornek@ibu.edu.ba*

Abstract

Hepatic coma, also known as hepatic encephalopathy, is loss of consciousness as a result of liver failure. Hepatic coma represents the final stage of hepatic encephalopathy - grade IV, a progressive brain dysfunction due to accumulation of substances toxic to the brain. Hepatic coma can rapidly progress and may ultimately lead to death. Therefore, early diagonosis of hepatic coma is consirerably crucial for patients' life. If not, patients with hepatic coma can die in few days. In this study, I have proposed to overview early diagnosis of hepatic encephalopathy by breath analysis using electronic noses which are regarded as rapid, inexpensive way of gas detection.

Keywords: Electronic nose, hepatic coma, sensor arrays, neural Networks.

1.INTRODUCTION

Hepatic coma is loss of consciousness as a result of liver failure. The brain is poisoned by toxic substances due to failure of the liver functionality. The toxic substances are generated after accumulation of some byproducts of metabolism in the blood.

The severity of encephalopathy is subdivided into four grades. Grade I and II are subtle symptom of brain. In grade III, significant brain damage occurs. Hepatic coma represents the final grade - grade IV of the brain dysfunction that toxic substances are collected in the brain. At this stage, the entire brain is damaged and the patient with hepatic failure becomes unconscious and is unable to respond to painful stimuli (hepatic coma). Ultimately, it may cause death. [1]

Studies have revealed that in patients with advanced stages of encephalopathy resulting froim chronic liver failure, ammonia, regarded as toxic substance, levels in the brain may rise more than twentyfold [2]. Blood tests show an increase in ammonia levels, which is a marker the degree of accumulation of toxins in the brain as well.

For the essence of patients health, early diagnosis of hepatic coma is vital. If early intervention is not committed, hepatic encephalopathy can rapidly progress and become an acute emergency condition regarded as coma causing death in a few days.

Current methods of diagnosis of the hepatic coma such as computed tomography scans are time-consuming, expensive, and involve invasive confirmation. The needs of rapid and

inexpensive methods have led researchers to find new techniques on the hepatic coma symptoms.

Electronic nose is a device formed by an array of sensors which is capable of highly sensitive for detecting and identifyig VOC's. Various studies have been conducted to identify various diseases using electronic nose with common pattern recognition algorithms. This study suggested that an electronic nose would detect and identify hepatic encephalopathy at advanced grades on the basis of the complex smellprints of numerous VOC's in exhaled breath from patients with hepatic encephalopathy

The breath of a healthy person gives a different pattern than that of a one with failure. This difference could be detected and classified by the electronic nose and an appropriate pattern classification algorithm such as Neural Network and SVM. The main objective of this paper is to suggest that it is possible to recognize individuals affected by advanced stage of hepatic encephalopathy called hepatic coma, analyzing the olfactory signal of their breath by the use of an electronic nose with an appropriate classification algorithm.

2.VOC's as a Biomarker of Certain Diseases

Since 1971, it has been well known that hundreds of VOCs are present in the human breath [3], and that some of these compounds are biomarkers or indicators with certain diseases. Metabolic changes within hepatic failure can lead to changes in the production of different volatile organic compounds [4] which may be detected in the samples of exhaled breath.

Over the last two decades, many studies on breath analysis by combined gas chromatography–mass spectroscopy (GC–MS) have been conducted that several hundreds of different compounds in human breath was found. They reported that some volatile compounds in the breath are associated with certain diseases. For example, in the breath of patients with liver cirrhosis mercaptans and aliphatic acids were identified[5] while in the breath of uremic patients dimethyl- and trimethylamine were found [6]. Similarly, ammonia, manganase and mercaptans quantity in the blood are accepted as biomarkers of hepatic coma or hepatic failure.

In addition, alkanes are present in the lung cancer and formaldehyde in the breast cancer; the presence of isoprene in human breath is correlated to blood cholesterol levels; and patients with Type 1 diabetes have excess acetone in their breath. [7]

3.The VOCs in the patients with liver disease

Dimethyl sulfide, acetone, 2-pentanone and 2-butanone are considerably high level in the breath of liver patients. These chemical compounds are the reason of bad smell of the breath. Sulfur containing compounds are produced by disfunctioned metabolism of sulfur containing amino acids in the transamination body system. Normally, the amount of these compounds in blood and alveolar breath are low. Dysfunction of liver increases the level of these compounds, which have a characteristic smell, like the smell of rotten cabbage.

The increased levels of the ketones acetone, 2-pentanone and 2-butanone are regarded to be the result of hepatic insuline resistance, a common disorder in patients with hepatic steatosis and end stage liver disease. Insuline resistance leads to an increase of triglycerides and free fatty acids and ketones are formed during lipolysis. Moreover, in a study with rats, the

amounts of these compounds increase because of the inhibition of certain enzymes in the liver.[8]

The correlation between a biomarker and a specific disease is often multi-fold. A breath compound can be a biomarker of about more than one disease or metabolic-disorder. And one particular disease or metabolic disorder can be identified by more than one chemical compounds. Table 1 shows correlation certain diseases and compounds.

Table 1. 35 established biomarkers and their physiological symptoms.[7]

Biomarkers	Metabolic Disorders / Diseases
Acetone (OC(CH3)2)	Lung cancer, diabetes, dietary fat losses, congestive heart failure, brain seizure
Acetaldehyde (CH3CHO)	Alcoholism, liver related diseases, lung cancer
Ammonia (NH3)	Renal diseases, asthma
Butane (C4H10)	Tumor marker in lung cancer
Carbon monoxide (CO)	Oxidative stress, respiratory infection, anaemias
Carbon disulphide (CS2)	Schizophrenia, coronary, and artery diseases
Carbon dioxide (CO2) (13C-Isotopes)	Oxidative stress
Carbonyl sulfide (OCS)	Liver related diseases
Ethane (C2H6)	Vitamin E deficiency in children, lipid peroxidation, oxidative stress
Ethanol (C2H5OH)	Production of gut bacteria
Ethylene (C2H4)	Lipid peroxidation, ultra violet radiation damage of skin

Hydrogen (H2)	Indigestion in infants, intestinal upset, colonic fermentation
H/D isotope	Body water
Hydrogen peroxide (H2O2)	Asthma
Hydrogen cyanide (HCN)	Pseudomonas aeruginosa in children affected with cystic fibrosis
8-Isoprostane	Oxidative stress
Isoprene	Blood cholesterol
Methane (CH4)	Intestinal problems, colonic fermentation
Methanethiol (CH3SH)	Halitosis
Methanol (CH3OH)	Nervous system disorder
Methylated amines	Protein metabolism in body
Methyl nitrate (CH3NO3)	Hyperglycemia in Type 1 diabetes
Nitrogen monoxide (NO)	Asthma, bronchiectasis, hypertension, rhinitis, lung diseases
Nitrotyrosine (C9H10N2O5)	Asthma
Oxygen (O2)	Respiration
Pentane (C5H12)	Peroxidation of lipids, liver diseases, schizophrenia, breast cancer, rheumatoid arthritis
Pyridine (C5H5N)	Periodontal disease
Sulfur compounds	Hepatic diseases and malordor, lung cancer
Hydrocarbons (Toulene (C6H5CH3), Benzene (C6H6), Heptane (C7H16), Decane (C10H22), Styrene (C8H8), Octane (C8H18), Pentamethylheptane (C12H26))	Lipid peroxidation, lung cancer, oxidative stress, airway inflammation

4.Electronic Nose

An electronic nose is an instrument which is composed of an array of electro chemical sensors with partial specificity and an appropriate pattern recognition system, is able to detect and identify simple or complex odors.

Electronic noses have been mainly used for quality control applications in the food, beverage, and cosmetics industries, military, and medical applications. As an odor is presented to the electronic nose, certain sensors are sensitive to the odor; therefore they respond to certain volatile componds. This combination of varied responses from the array of sensors constitutes the characteristic of the particular applied odors. After presence of analyte the output of the odor sensors is extracted, amplified, filtered, and converted into digital form by transducion electronics.

Compared to traditional analysis techniques, electronic noses have certain motivations. The main motivation for electronic noses is capable of inexpensive, rapid, real-time as well as portable and reproducible measurements of volatile compounds.

However, a universal electronic nose has not been built yet, which is capable of identifying or discriminating any gas sample type with high efficiency and for all possible applications. Because it is highly depends on the selectivity and sensitivity limitations of electronic nose sensor arrays for particular analyte gases. Therefore, electronic noses are not univerally utilized for every application of the gas samples. A proper electronic nose for a particular application should meet an evaluation of mecanism.

5.The Biological Nose

The human olfactory system comprises variety of chemical sensors, known as receptors, and automated pattern recognition incorporated into the olfactory bulb and olfactory cortex in the brain [9, 10]. A receptor type alone can not identify a specific odor. It is the set of receptors composed of pattern recognition that can detect and identify each odor. Fig.3 shows the main components and function of the human olfactory system and its sensory components. Once odor molecules are presented to the olfactory receptors stimulating an electro-chemical response that is transmitted through the crib form plate to the olfactory bulb and ultimately the olfactory cortex.

The olfactory receptors (sensors), the olfactory bulb (signal pre-processing), and the olfactory cortex (odor identification) are the major olfactory components in human olfaction system.

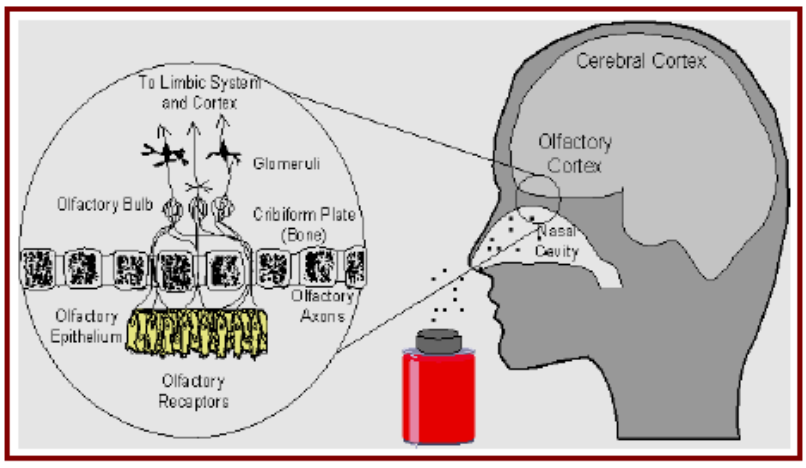

Figure 3. Human Olfaction Sensing System [11]

6.Sensor Technologies on Electronic Nose

Metal Oxide Semiconductor (MOS) was the first developed sensor array, which detected 20 odours [12]. By the technological development sensor arrays are created from six up to 32 sensors with different materials, detecting thousands of smells. This equipment varies different types of sensors interacting with volatiles: Metal Oxide Semiconductor Field Effect Transistors (MOSFETs), Quartz Crystal Microbalances (QCMs), the Surface Acoustic Waves (SAWs), Conducting Organic Polymer Sensors (CPs), Intrinsically Conducting Polymers (ICPs) and optical fiber bundles . Modern electronic noses (e-noses) can be constructed with more than one type of sensor in them. [13]

7.CONCLUSION

Up to date, many papers on medical research using electronic nose have been studied. Neural network is the appropriate pattern recognition method for identifying patients with hepatic failure and healty individuals. As medical sensing samples are non linear, the most appropriate classificatiton method is neural which can train and test non linear medical samples in a short time with high accuracy compared to other algorithms.

One of key factor for sensing odor is using the appropriate sensor. After a long time research, it is believed that polymer film coated sensors are more suitable for the medical diagnosis usin electronic noses.

As a result electronic noses are prominent system as non invasive method of medical diagnosis. The studies have been shown that with appropriate sensor arrays and corresponding pattern recognition, electronic nose can be widely used for many diseases. Therefore, for early detection of hepatic coma, patients with hepatic failure can be efficiently analyzed by electronic nose for detection and identification.

REFERENCES

1. http://www.nmihi.com/h/hepatic-coma.htm

2. Butterworth, R. F., Pathophysiology of hepatic encephalopathy: A new look at ammonia. Metabolic Brain Disease 17: 221-227, 2002

3. Pauling, L.; Robinson, A.B.; Teranishi, R.; Cary, P. Quantitative analysis of urine vapor and breath by gas-liquid partition chromatography. Proc. Nath. Acd. Sci. USA 1971, 68, 2374-2376

4. Mazzone, P., Hammel, J., Dweik, R., Na, J., Czich, C. Laskowski, D., & Mekhail, T., Lung Cancer Diagnosis by the Analysis of Exhaled Breath with a Colorimetric Sensor Array. ,2007

5. Kaji, H., Hisamura, M., Sato, N., Murao, M., 1978. Clinica Chimica Acta 85, 279

6. Simenhoff, M., Burke, J., Saukkonen, L., ordinario, A., Doty, R., 1977, New England Journal of Medicine, 297,132.

7. Wang, C., Sahay, P., 2009, Breath Analysis Using Laser Spectroscopic Techniques: Breath Biomarkers, Spectral Fingerprints, and Detection Limits, Sensors ISSN 1424/8220

8. Velde, V.D., Nevens, S., Hee, F.V., Steenberghe, P.V., Quirynen, D.; 2008, GC-NS analysis of breath odor compounds in liver patients, Journal of chromatography b-analytical Technologies in the biomedical and life sciences vol:875 issue:2 ,344-348

9. Merler, S., C. Furlanello, B. Larcher and A. Sboner, 2001. Tuning Cost Sensitive Boosting and its Application to Melanoma Diagnosis, In MCS 2001, Cambridge, UK, 2096: 32-42.

10. Pardo, M. and G. Niederjaunfner, 2000. Data Preprocessing Enhances the Classification of Different Brands of Espresso Coffee with an Electronic Nose. Sensors & Actuators B, 69.

11. Shilbayeh, N.F. and M.Z. Iskandarani, 2004. Quality Control of Coffee Using an Electronic Nose System. Am. J. Applied Sci., 1: 129-135.

12. Persaud, K.C.; Dodd, G. Analysis of discrimination mechanisms in the mammalian olfactory system using a model nose. Nature 1982, 299, 352-355.

13. Casalinuovo IA, Di Pierro D, Coletta M, and Di Francesco P. 2006. Application of electronic noses for disease diagnosis and food spoilage detection. Sensors 6:1428–1439.