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BRAIN ACTIVATION EXPERIMENTS WITH 99mTc HMPAO SPECT

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ÖZET:

Bu çalışmada İngiliz dilini farklı düzeylerde bilen deneklerle bir dizi beyin aktivasyon deneyleri yapılmıştır. Deneklerin beyin metabolizmaları beyine verilen dili kullanmayı sağlayıcı bir takım görevler sonucu değişen kan akışkanlıklarını belirleme yoluyla ölçülmüştür. Bu çalışmaların tümü Türkiye'de ilk defa Gazi Üniversitesi Hastanesi, Nükleer Tıp Anabilim Dalı 'nda gerçekleştirilmiştir. Deneylerde kullanılan metod 99mTc HMPAO (Hexamethylpropylene Amine Oxime) S.P.E.C.T. (Single Photon Emission Computerized Tomography) olarak adlandırılmaktadır. Deneylerin tümünde radyoaktif bir elementle (Tecnetium) bağlanan ve beyin görüntülemede kullanılan ,bir madde (Hexamethylpropylene Amine Oxime) intravenöz yolla vücuda uygulanmıştır. Radyoaktif bir elementle bağlanmış beyin perfüzyon ajanı direk olarak beyine ulaşmış ve beynin gama ışını yaymasını sağlamıştır. Yayılan gama ışınları dönel gama kameraları ile toplanmış ve bir takım bilgisayar destekli işlemlerden sonra renkli beyin görüntüleri elde edilmiştir. Deneklerin İngiliz dili seviyeleri ve uyrukları sırasıyla şöyle sıralanabilir: 1. Orta (Türk), 2. İleri Seviye (Türk), 3. İki Dilli (Türk ve İngiliz), 4. Anadil Konuşucusu (Amerikan). Başlıca bazal ve aktivasyon olmak üzere ikiye ayrılan deneylerin bazal bölümlerinde deneklere yukarıda sözü edilen beyin perfüzyon sintigrafisi ajanı enjekte edilmiş ve deneklerin beyinlerini dil açısından aktive etmeyecek bir ortamda gama SPECT kameralarıyla beyin görüntüleri çekilmiştir. Başka bir günde gerçekleştirilen aktivasyon çalışmalarında ise denekler 50 sorudan oluşan ve sözel dil yeterliliğini ölçen bir sınava tabi tutulmuşlardır. Buradaki sözel sınavla deneklerin beyinleri dil fonksiyonları açısından aktif hale getirilmiştir. Sınavın yaklaşık ortalarına doğru, bazal çalışmada da kullanılan aynı beyin perfüzyon ajanı deneklere enjekte edilmiş ve denekler soruları cevaplandırmaya devam etmişlerdir. Soruların yanıtlanması bittikten sonra deneklerin tekrar gama kameralarıyla beyin görüntüleri elde edilmiştir. Karşılaştırmalı çalışmalara ölçüt oluşturan bazal görüntülerle dil aktivasyonlarını gösteren aktivasyon görüntüleri arasında orta düzeyde İngilizce bilen denek dışındaki deneklerde önemli bir beyin perfüzyon artışı görülmemiş, ancak orta düzeyde İngilizce bilen deneğin beynindeki tüm frontal kortekste ve özellikle sol bölgede bir perfüzyon artışı görülmüştür.

ANAHTAR SÖZCÜKLER: SPECT görüntüleri, HMPAO (Hexamethylpropylene Amine Oxime), beyin perfüzyonu, nükleer tıp, dil edinimi ve öğrenimi.

Not: SPECT metoduyla uygulamalı nörodilbilimsel çalışmada çekilen ve renk kodlarının önemli olduğu renkli beyin grafileri dergide renkli fotoğraf basılamamasından dolayı makaleye ilave edilememiştir.

ABSTRACT:

The purpose of this study is to obtain physical evidence which differentiates four levels of language in right - handed subjects whose levels of English language are intermediate, advanced. bilingual and native. The brain metabolisms of the subjcets were investigated in the light of the changing regional cerebral blood flows according to the language tasks given to the subjects. The method applied in the experiments is termed as 99mTc HMPAO (Hexamethylpropylene Amine Oxime) S.P.E.C.T (Single Photon Emission Computerized Tomography). This method also necessitates intravenous injection of a radioactive element (Technetium) which is linked with a pharmaceutical Hexamethylpropylene Amine Oxime that is specific to brain. The injected substance emits gamma radiation which are detected by the gamma cameras and then turned into colored brain images. The language levels of English and the nationalities of the volunteer subjects are: 1.Intermadiate (Turkish). 2. Advanced (Turkish), 3. Bilingual (British and Turkish), 4. Native Speaker (American). The experiments comprise the baseline and activation phases. The subjcets were injected the brain perfusion agent 99mTc HMPAO first and their brain images were performed with a rotating gamma camera in the baseline phase. In the activation studies, the volunteers were given a 50 question oral language proficiency test showing gradual difficulty. Approximately in the middle of the test, the subjects were injected the perfusion agent and they kept answering the questions. After completing the test, their brain images were taken in the same way. It can be pointed out that between baseline and activation studies there were no differences among the subjects except the volunteer whole language level of English was intermediate. It was also seen that the whole frontal cortex, particularly the left side, revealed increased brain perfusion in this volunteer subject.

KEY WORDS : SPECT images, HMPAO (Hexamethylpropylene Amine Oxime), brain perfusion, nuclear medicine, language acquisition and learning.

Note: The colored SPECT images that were performed in this applied study are not added to the article because it is impossible to print colored photographs in this journal.

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1. INTRODUCTION

1.1. The Human Brain and Language

It is an undeniable fact that the human brain is the most complex organ by the help of which the differentiation of human beings from the other living beings is made possible. There are still many unknown facts about human brain though the computer-based medical innovations. On the cortex of human brain, there are some parts that are special for certain cognitive functions. Language is one of those functions and makes us human beings in nature. When compared to the other communication systems of species, human communication systems is the most complicated one in the world.

Linguistics can be divided into two categories; microlinguistics and macrolinguistics. Microlinguistics which deals with the structure of language systems can be further divided into four subcategories; phonetics and phonology, morphology, syntax and semantics. Macrolinguistics, on the other hand, studies all sorts of vital things which are about language and languages. Macrolinguistics has several developing subdivisions like sociolinguistics, psycholinguistics, stylistics, computational linguistics, biolinguistics, neurolinguistics etc. [1]. Neurolinguistics is sometimes called as neurological linguistics. It examines the neurological aspects of language processing in human brain. In addition, it tries to create a model of brain responsible for speech and hearing [2]. Fromkin [3] also points out that, "The attempt to understand what makes language acquisition and use possible has led to research on brain mechanisms and the relationship between the brain and language. The study of this relationship is called neurolinguistics."

Furthermore, neurolinguistics investigates the relationships between language and brain. Besides, neurolinguistics investigates the areas basically related to language in the human brain together with clinical linguistics on speech disorders and aphasia . There are many contributions of other sciences to neurolinguistics. These fields can be listed as follows; clinical aphasiology, neurosciences, biology, anthropology, philosophy, psychology, psychiatry, neurology [4].

In addition, neurolinguistics is related to the fields about cerebral dominance of language, neuropsychological models of language, language disorders and speech therapy, and forming bases for artificial communication systems [5]. There is also applied linguistics which is the application of linguistic facts to practical fields. The term neurolinguistics can also be categorized according to applied linguistics limitting the other disciplines, for example, sociolinguistics, psycholinguistics, biolinguistics, computational linguistics, stylistics, and information theory [6]. By the help of applied linguistics, facts on neurolinguistics can be applied in the aspect of language teaching and the departments of language teaching and linguistics notably in academic life. Modern methods of speech therapy can be further developed in the light of neurolinguistics. It is a fact that in recent years, neurolinguistics has been growing rapidly via the great contributions of medical developments and computer technology, for instance nuclear imaging.

Kandel [7] points out that the scientific study of learning, memory and language give information about how knowledge is processed in the brain. As a first step, there were several studies in order to clarify the neural mechanisms in the light of clinical neurology. The following phase comprises the localization of speech but which is not sufficient for understanding the neural mechanisms of language.

The studies on the relations between language and the brain is not a new field investigated in this century. Lesser [8] notes that the historical background of examining the language processing in the brain started approximately 5000 years ago. An Egyptian papyrus written in 3000 B.C. showed that injuries to the temple of the head is responsible for speech disorders. On this papyrus, the ancient Egyptian scientist Imhotep, put forward the importance of the damaged area. Ornstein [9] notes that the French physician Marc Dax found that losing ability to speak results from the damage to the left side of the brain, or so called aphasia. Dax also concluded that all of the patients suffered from lesions in the left hemisphere, and he put forward his proof in a medical meeting in France in 1836 on left hemisphere dominance for language. However, Dax could not get enough concern. In 1861, the French neurologist Pierre Paul Broca investigated the human brains suffering from speech loss. He found that all of the brains had damages in a certain area of the left frontal lobe. Arnold [10] mentions that damages to the area presented by Broca result in aphasia. In 1874, Wernicke found that damages to the left cortex next to the auditory area result in disorders of comprehension .

In the past twenty years, examination of human brain for the language functions rapidly developed by the help of the application of some devices such as magnetic resonance imaging. Besides, PET (Positron Emission Tomography) scans made it possible to investigate the brain functions of human brain in performing linguistic tasks [11]. In fact, there are still many unknown things on human brain and language, for instance, the ways of storing concepts in

the human brain. It should be kept in mind that, although the structures forming words and sentences have been investigated since the nineteenth century, these structures are not explained totally in today's contemporary medical methods.

1.2. The Aim and the Method of the Study

The aim of the experiments is to get the neurological supports that differentiate four levels of English language in the volunteer subjects who know English as a foreign language and to compare them with native and bilingual ones. The regional cerebral blood flows of the volunteers were examined through 99mTc HMPAO (Hexamethylpropylene Amine Oxime) SPECT (Single Photon Emission Computerized Tomography) method in the Department of Nuclear Medicine of Gazi University Hospital. The applications consisted of two steps, baseline and post-activation studies. In the baseline study, the volunteer subjects were injected the radioactive brain perfusion agent termed 99mTc HMPAO and their SPECT images were taken. In the other phase, the subjects were given an oral proficiency test of which questions revealed gradual difficulty. The same brain perfusion agent was injected to the volunteers approximately in the middle of the test and they kept on answering the questions. Having completed the test, the SPECT images of the volunteers were taken as well.

1.3. Contributions and Difficulties

Needless to say, the experiments were done with the medical contributions and assistance of the Department of Nuclear Medicine of Gazi University Hospital. From the standpoint of the volunteer subject selection, the experiment team had great difficulty because of the fact that the volunteer subjects would be injected the brain perfusion agent containing radiation. Thus, many of the candidate subjects got scared when they heard the term nuclear although the amount of radiation was so low. It is a fact that finding enough subjects in these studies is a great problem for the researchers. It was a notable chance for the experiment team that four subjects were found.

SPECT machines are extensively used mostly for diagnostic purposes in medicine, for example, in neuro-psychiatrical and pathological studies. However, this study, applied via nuclear medicine, is the first study in the aspect of applied neurolinguistics. It is hoped that this work will enlighten the way for the following neurolinguistical studies through nuclear medicine.

2. BRAIN ACTIVATION EXPERIMENTS

2.1. Subject Selection

There are four volunteer subjects in the brain activation studies. Their levels of English are as follows: 1.Intermediate, 2. Advanced, 3. Bilingual, 4. Native American. First of all, the candidate subjects were informed about the aim of the study and given medical resources on nuclear medicine. There were approximately ten people who were asked to participate in the experiments. However, only four people accepted to take part in the studies. The four subjects filled in the information sheets about them and they signed the petitions in which they stated that they would like to participate in the experiments voluntarily and for the sake of science.

2.2. Difficulties and Criteria in the Selections

The term "NUCLEAR MEDICINE" is misunderstood by most people. When they hear the word nuclear, they think that the amount of radiation is fatal. In this context, finding enough subjects was a great problem for the experiment team as is noted before. Another important point is that neither the subjects nor their relatives suffer from any neuro/psychiatric diseases, for instance schizophrenia. Because the brain blood flow of a person suffering from a neuro/psychiatric illneess is different from a normal person's brain blood flow which is so significant for the study. In order to obtain accurate results, the volunteers should not use any drugs. Moreover, the subjects were asked not to drink neither alcohol nor coffee or tea, and also asked not to smoke cigarettes or take pain killers before the experiment, all of which change the normal blood flow of the brain.

Another key issue is that the female subjects should not be pregnant due to the fact that the radiation that is injected to the body may be dangerous for the baby. In addition, the subjects should be all right handed meaning that mostly they have their speech centers in the left hemispheres of their brains.

2.3. SPECT Studies

The brain activation experiments were done with a dual headed SPECT camera, at the Department of Nuclear Medicine in Gazi University Hospital. Assessments were done in a quiet and semi dark room with eyes open. 99mTc HMPAO was used as a perfusion agent. Commercially available kits (Ceretec - Amersham International U.K.) were labeled according to manufacturer's instructions. SPECT study consisted of two steps, baseline and activation.

2.3.1. Baseline Phases

In the baseline studies, the subjects were not given any language tasks in order that their brains would not get activated in terms of language. They were injected 99mTc HMPAO intravenously (the amount of radiation is approx. 15 milicurie per in-

jection) and they laid down under the SPECT instrument. The two headed gamma camera started rotating 360 o (full angle tomography) and capturing the emitted gamma radiation from the brain. By the help of the other digital devices and computers emitted gamma radiation was then turned into colored images which formed base criterion for the activation studies.

2.3.2. Activation Phases

In the activation phase, the subjects were given an oral proficiency test in order to activate the language centers in their brains and to evaluate the brain metabolism. The interviewer scored the answers in accordance with grammar-sentence structure, pronunciation and ability to communicate. Approximately in the middle of the test, the subjects were injected the same brain perfusion agent by the help of a medical instrument termed intracath by the help of which the vein passage was kept open. Except the first intermediate level subject, all of the subjects gave accurate and fluent answers to the questions. After the completion of the test, the subjects were taken to the SPECT room and they laid down under the SPECT instrument. The rotating gamma camera again captured the emitted gamma radiation and then turned into colored images. The images revealed the brain activation nearly 2-3 minutes after and before the injection.

2.3.3. Image Reconstruction and Interpretation

After the image reconstruction was performed, transaxial slices were obtained parallel to orbito meatal line. Transaxial, coronal and sagittal slices were generated and the slices were analyzed visually. Interpretation of the SPECT scans was performed quantitatively by reviewing the images on a computer screen as well as the recorded hard copy files independently by two experienced physicians. All baseline transaxial slices of the volunteers revealed normal findings. In the activation study, frontal and parietal lobes of the first intermediate level volunteer showed increased brain perfusion. Transaxial slices of the other volunteers revealed normal findings again.

3. DISCUSSION

It is an undeniable fact that nuclear medicine is in the service of neurolinguistics which investigates the relations between brain and language. By the help of nuclear medicine, it has become so easy to exhibit the related areas where language and memory functions are placed.

According to the SPECT images of the volunteers, there is a notable increased brain perfusion in the first intermediate-level volunteer subject. The first subject has been studying English for almost 1 year with systematic instruction and she answered approximately the half of 50 questions. At first, she gave accurate and fluent answers to the simpler questions, for instance, "How are you?" For the more difficult questions she could not articulate the answer although she understood them. For instance, "Most of us have no difficulty in expressing ourselves when we are having a conversation with a friend. How does a conversation with only one or two people differ from a public speech? Give several examples to illustrate the differences."

The first subject had no difficulty in answering the simpler questions, in other words, her Wernicke's and Broca's areas worked synchronously. During answering the more difficult questions, although her Wernicke's area decoded the messages, she was not able to utter vocally through the Broca's area. Moreover, for the most difficult questions, she neither understood the questions nor gave any answers. In this context, it can be noted that, in answering session, her Wernicke's and Broca's areas consumed energy, in other words, oxygen and glucose consumption leaded into increased brain perfusion in the left side of her frontal and parietal cortexes.

The second advanced level subject has been studying English for almost sixteen years. She is attending the English Language Teaching Department of Hacettepe University and she is a professional tourist guide. Although she was given systematic instruction in the early years of studying English, she was exposed to a rich medium of English particularly due to her profession and education. Increased brain perfusion in the speech centers of her brain was not determined.

As for the bilingual subject, her answers were both accurate and fluent. Besides, she made further philosophical comments on the questions. She knows both English and Turkish very well due to the fact that she has been exposed to Turkish from his Turkish father and British from her mother who is a native speaker since her birth. There was no change in her regional cerebral blood flow because of her high performance of English. Like the advanced and the bilingual subjects, the last native American subject did not have any problems in answering the questions. Again he made further comments on the questions. No increased perfusion was seen in his activation images.

According to the results of the volunteer subjects, we may speculate that the speech centers for both native and the second language were the same on the cortex. In other words, the same areas of speech are responsible for more than one language. More-

over, if one person's knowledge of foreign language, for example English, is not sufficient he or she uses the language areas more, that is, the cerebral blood flow increases in accordance with the given language tasks. The speech centers try to encode and decode a foreign language of which semantic, syntactic and phonemic forms are not so familiar for the language cortex.

For the second advanced level subject, due to her being exposed to English over long years, her brain got used to becoming familiar with the syntactic and semantic patterns of English language. It can be mentioned that being exposed to a foreign language in a long period with a comprehensible and meaningful input leads to accurate and fluent utterance without an extra effort. For the bilingual and the native volunteers, it can be said that they have been exposed to English language since their birth. They acquired the language without a systematic instruction and unconsciously during a period in which their brains got plasticity. This period that is between age two and puberty is termed as the critical period as noted by Lenneberg [12]. In this context, it can be pointed out that learning and teaching a foreign language should start at an earlier age. As is noted before, the volunteers who started learning English at an earlier age did not show additional performance in speaking and understanding the language. It is a fact that being exposed to the foreign language in a meaningful context results in using the foreign language effectively.

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