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Dancing with the Waves

Highlights

A Cross-Sectional Study

Intractable Epilepsy Surgery

Discovering Thoughts, Inventing Future

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Dancing With the Waves: A Case Report

By Dr. Amr Guenedi, Dr. Yousif A. Obeid & Ala'Aldin Alhussaini
Sultan Qaboos University, Oman

Summary- This case presentation describes a 19 years old female presenting with episodes of abnormal behavior in the form of singing and dancing. We assessed her mental and physical status as well as fully investigating her condition. She was diagnosed as Frontal lobe epilepsy and had shown good response to Lamotrigine.

GJMR-A Classification : *NLMC Code: WW 400, WB 141*

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Dancing With the Waves: A Case Report

Dr. Amr Guenedi [α], Dr. Yousif A. Obeid [σ] & Ala'Aldin Alhussaini [ρ]

Summary- This case presentation describes a 19 years old female presenting with episodes of abnormal behavior in the form of singing and dancing. We assessed her mental and physical status as well as fully investigating her condition. She was diagnosed as Frontal lobe epilepsy and had shown good response to Lamotrigine.

I. Introduction

Epilepsy is the most common serious neurological condition with a varying degree of impact on patients' lives. Its prevalence is around 5-10 per 1000, slightly more common in males than females. The complexity of the disorder in the form of varying symptoms and underlying brain pathology makes the diagnosis and management challenging at times. Clinicians should always bear in mind such diversity of presentation so as not to miss such cases.

II. The Case

Our current case is a 19 years old female with 3 years history of episodes of change in behavior. The episodes constitutes of singing loudly, clapping of her hands and humming a musical tone. There was laughing and dancing as well. Each episode lasts ½-1 minute, ending suddenly, leaving the patient very low thereafter. These episodes were not provoked and not preceded by an aura. They were occurring about one to two times per week. Her social life was significantly affected by these episodes.

The episode was witnessed in our outpatient clinic. Of course most of the attendants were shocked by such a behavior considering her cultural background. During the episode she is conscious about the behavior but cannot stop it. No associated incontinence or tonic clonic seizures.

Between the episodes she is quite normal with good sleep and appetite. She has no psychotic or obsessive features, and her mood is reactive except for some degree of anxiety concerning her condition.

Family history & past medical history were uneventful: there was no past history neither of serious medical illness, febrile convulsions or head trauma. The patient was not on any medications.

As regard her personality, she was known to be generally cheerful with many friends at school. She had a stable academic performance.

a) Mental state examination

i. *Appearance & behavior*

She was a well- dressed young lady. She was cooperative with good eye contact. There were no abnormal movements (except those during the attack). Speech: her speech was coherent, of normal, rate and rhythm

ii. *Mood*

Her mood was reactive.

iii. *Perception and thinking*

There were no illusions or hallucinations, no depersonalization or derealization, there were neither delusions nor obsessive thoughts.

iv. *Orientation & Memory*

She was well oriented to time, place and person, with good attention and concentration. Her immediate, short and long term memory were intact.

v. *Insight*

Insight was preserved.

b) Physical examination

Normal Physical Examination including full neurological examination and fundoscopy.

c) Investigations

She was fully investigated including CBC, U/E, LFT, TFT, CT brain and serum calcium Were all normal.

A wake EEG did not reveal any abnormality but a Sleep EEG showed epileptic form discharges on the frontal regions.

d) Differential diagnosis[2]

- Metabolic disorders (e.g. hypoglycemia, hyponatremia).
- Migraine
- Transient ischemic attack.
- Frontal lobe epilepsy
- Temporal lobe epilepsy
- Absence seizure
- Psychogenic non-epileptic seizure
- REM behavior disorder
- Conversion disorder
- Panic attacks
- Malingering.

She was thus labeled as Frontal lobe epilepsy.

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e) Management and follow up

She was started on Lamotrigen and the dose was built up to 50mg BD with good response. After six months she presented with increase in the number of episodes associated with urinary incontinence.

The dose of Lamotrigen was increased to 100mg BD with good control. She was followed in OPD with good control.

After 2 years of being symptom free, the dose of Lamotrigen was gradually reduced till it was totally stopped. This was followed by an EEG, which was reported as normal.

It's worth mentioning that during the period of treatment her scholastic achievements were constant.

III. Discussion

The Frontal lobe is divided into three main parts. The Premotor Area which plans any type of Movement, Motor area which executes the movement and the Prefrontal region where functions like mood, emotions, Behaviour as well as some cognitive functions are harbored. Frontal lobe epilepsy is an abnormal discharge in the frontal region leading to partial or generalized seizure activity. Because of the functions carried out by this part of the brain such abnormal activity can lead to a diversity of symptoms. These can be motor, behavioral or both. The differential diagnosis thus includes psychiatric disorders as well as medical organic causes. Hence neurologists and psychiatrists may be faced with such exercise in diagnosing Frontal lobe epilepsy {4}.

In our case the nature of the symptoms, observing the symptoms with the disinhibtion raised the suspicion of frontal lobe pathology. This is confirmed by the sleep EEG. The response to Lamotrigine was very good with almost no side effects.

IV. In Conclusion

We reported a case with Frontal lobe epilepsy presenting with both behavioral and motor features. She was diagnosed after witnessing an episode in the clinic and performing a sleep EEG. She had shown good response to Lamotrigine.

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Motor and Oculomotor Performance Assessment in Infants in Primary Health Care Level: A Cross-Sectional Study

By Silvana Alves Pereira, Vanessa Braga Torres, Ingrid Fonsêca Damasceno Bezerra, Marina Pegoraro Baroni, Johnnatas M. Lopes, Cristiane A. Moran & Marcelo F. Costa
Universidade Federal do Rio Grande do Norte, Brazil

Abstract- *Objective:* Assess the oculomotor and motor performance of infants without neonatal risk factors.

Method: Twenty six term infants without neonatal risk factors were selected. Infants were six months old when they had their motor and oculomotor performance assessed respectively using the Alberta Infant Motor Scale and the Optokinetic Nystagmus, this latter was assessed using a drum with white and black stripes interspersed with each other. Ratings were recorded on video and motor and oculomotor performances were assessed and scored by two evaluators who have been trained and are blind to the study. For data analysis, X2 for reliability analysis and the Mann Whitney test for correlation of continuous variables. The significance level was 5% for every analysis.

Results: It was found 15% of assessed infants showed motor development abnormalities and only one infant showed no Optokinetic Nystagmus movement.

Keywords: *infant, child development, risk factors, term birth, ocular movements, optokinetic nystagmus.*

GJMR-A Classification : *FOR Code: WL 103, WL 140*

Motor and Oculomotor Performance Assessment in Infants in Primary Health Care Level: A Cross-Sectional Study

Silvana Alves Pereira [α], Vanessa Braga Torres [σ], Ingrid Fonsêca Damasceno Bezerra [ρ], Marina Pegoraro Baroni [ω], Johnnatas M. Lopes [¥], Cristiane A. Moran [§] & Marcelo F. Costa [χ]

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Conclusion: Term infants have abnormal motor performance and can present absence of optokinetic nystagmus.

Keywords: infant, child development, risk factors, term birth, ocular movements, optokinetic nystagmus.

I. Introduction

Although health has shifted from the biological field to the population living conditions, requiring direct and intersectional public intervention, the essential pursuit of improving life quality with peace, equity and social justice, and citizenship (Teixeira, 2000) the risks and neuromotor development delays evaluation is oriented mostly to a specific group of newborn infants (Carvalho, 2005), (Formiga, 2009) (Pereira, 2011), not being performed as a routine in primary health care.

The lack of surveillance systems, which complicates the identification and monitoring of vulnerable children, may be a possible explanation for this gap and the no use of appropriate tools to screen children at risk for motor neuropsychiatric development (Torburn, 1990). In addition, children living in developing countries often live in unfavorable family environments, where stimulation and social support are inadequate (Halpern, 1996). This sequence of events raises the risk of delay in their cognitive, physical and social development.

Within this perspective, new studies have already interpreted instruments as an alternative to assess the complexity of the child development process, in order to prevent and detect deviations and to establish strategies for early intervention (Gagliardo, 2003). Early detection is the main vehicle to monitor and adjust the physiological and pathophysiological function of various systems, such as the motor system, in all situations.

The Alberta Infant Motor Scale (AIMS) has been used in many studies in children, as it is considered a reliable and valid instrument for measuring motor performance and detect possible changes aiming to establish an early intervention (Syrengelas, 2010) (De Kegel, 2012) (Saccani, 2013).

The oculomotor performance assessment is quite simple, low cost (Ricci, 2008) and the possibility of timely detection of changes in the oculomotor system is connected to a timely diagnosis and prompt attention, thus favoring children and their families' life quality,
since there is a reciprocal relationship between visual and motor function (Pereira, 2011), (Saccani, 2009) (Mancini, 2002) (Halpern, 2000) (Saccani, 2010) (Cassidy, 2000).

The motor-visual reciprocity is represented by a complex set of interdependency between sensory system and ocular motility, and its muscle contraction command is determined by the central nervous system (Gagliardo, 2003) (Gagliardo, 2004) (Costa, 2007) (Mezzalira, 2005).

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This research objective was to assess the visual and motor responses of infants at primary health care level.

II. Method

A cross-sectional study was performed with infants born in Ana Bezerra University Hospital's Maternity (HUAB – Hospital Universitário Ana Bezerra), after the Committee of Ethics in Research approval, an integrant of Onofre Lopes University Hospital, within Federal University of Rio Grande do Norte, under the protocol number 77081/2012.

The sample, which have been drawn for convenience, consisted of six-months-old infants, born at term, weighing less than 2500g, by single delivery, without participating in intervention programs, having the free and enlightened consent by the person responsible (infant mother or guardian), which term was properly signed.

Infants excluded from the study showed neurologic diseases, orthopedic problems, sensory impairments (hearing and/or visual) and infants with Apgar value of less than five in the fifth minute.

In order to select the inclusion criteria, it was initially performed a retrospective analysis of infants medical records, which have been born between September/2011 and February/2012. At this stage, 180 charts were selected and 95 were analyzed. The data gathered included: date and type of delivery, Apgar scores, head circumference, infants' birth weight and length; as well as information relating to the mother (mother's age, marital status and occupation) and obstetric information (gestational age, parity, and gestational problems).

After analyzing the patient charts and approximately six months after the infant date of birth, a prior contact with the infant mother or guardian had been made by phone and/or home visits, to provide them with guidelines to participate in the research and to schedule the neuromotor performance assessment.

In order to assess neuromotor skills acquisition it was used the AIMS, which had been developed by Piper and Darrah (1992) (Piper, 1992). Based upon the literature, consists of 58 items grouped into four subscales that describe the development of spontaneous movement and neuromotor skills; these subscales are determined by four basic positions: prone, supine, sitting and standing (Carvalho, 2005) (Saccani, 2009) (Vieira, 2009) (Zajonz, 2008) (Mancini, 2004) (Zajonz, 2008) (Lima, 2004).

In each subscales' item, detailed descriptions of weight support, posture and antigravity movements observed in each position are included. At the end of the assessment it was credited a percentile, ranging from 5% to 90%. The percentile presented by summing the four subscales was used to rank neuromotor performance: normal/expected, exceeding 25% in percentile curve; suspect, between 25% and 5%; and abnormal, below 5% (Piper, 1992) (Mancini, 2004) (Zajonz, 2008) (Lima, 2004).

After the motor performance assessment, it was performed the oculomotor performance assessment with the infant sitting comfortably on the mat with his trunk being supported by the researcher.

In order to perform this assessment it was presented, 30 cm away from the infant, a target-shaped drum with interspersed white and black stripes, similar to optokinetic drum from Bárány (El Hassan, 2001). The drum was rotated in front of the infant in an attempt to attract his attention and assess the ocular movement called Optokinetic Nystagmus (Figure 01). The ocular movements promoted vertical measurements as stripes turned left and right, and horizontal measures, as stripes turned up and down. During the assessment the infant was expected to follow the drum movement presenting rhythmic repeated and involuntary oscillations movements of the eyes.

Figure 1

Figure 1 : Optokinetic Nystagmus assessment. The drum (radius 6.5 cm – 12.4° of visual angle and height of 17 cm – 31.6° of visual angle) with horizontal black and white stripes (4 cm each – 7.6 cycles per degree of visual angle was used for evaluation of optokinetic nystagmus. Was performed vertical measurements with the stripes rotating left and right and horizontal measurements, by rotating the stripes up and down. During the assessment it was expected the baby to accompany the drum's movement by presenting repeated and involuntary rhythmic, oscillating motions of the eyes (movements of smooth pursuit and saccadic movements of return).

At the end of the assessment the mother and/or guardian was requested to respond to a closed questionnaire, providing information regarding sociodemographic data. A single examiner, who was well trained to use the scale, has evaluated all children. Ratings were recorded on video and motor performances were reassessed and scored by two evaluators who have been trained and are blind to the study.

The collected data were archived using the Statistical Package for Social Sciences Program for Personal Computer (SPSS-PC) Program, version 17, and grouped according to the studied variables. For data analysis, the Shapiro Wilk test was performed for normality analysis, X2 for reliability analysis and the Mann Whitney test for correlation of continuous variables.

III. Results

Considering the total of 95 infants which were selected for the study: 26 were effectively assessed; 16 were not located, because there were no full address medical record entries; and 53 did not reside at the address identified in the medical record and/or had no telephone number.

All 26 infants were evaluated at six months of age (Median = 6.45 ± 0.37 m), were born with a gestational age between 37 to 41 weeks (Median = 40 weeks ± 1.11), average weight of 3459.42 g ± 382 and head circumference of 34 cm ± 1.27. Table 1 shows the sample characteristics.

Table 1 : Sample characterization

Characteristics	Assessed Group (n = 26)
Perinatal	
Mother's Age (year) – Mean (SD)	29 (±6)
Type Childbirth – f (%)	
Normal	15 (58)
Cesarean	11 (42)
Neonatal	
Sex – f (%)	
Female	15 (58)

Gestational Age (wk) – Mean (SD)	40 (±1,11)
Birth weight (g) – Mean (SD)	3459,42 (±382)
Birth height (in cm) – Mean (SD)	50 (±2)
Head Circumference (in cm) – Mean (SD)	34 (±1)
APGAR at 1 minute (score) – Mean (SD)	8 (±1)
APGAR at 5 minutes (score) – Mean (SD)	9 (0)
Exclusive Breastfeeding	
Yes	17 (65)
No	9 (35)

Caption: SD – standard deviation; f – frequency; % – percentage; wk – weeks; g – grams; cm – centimeters.

Regarding socioeconomic conditions 16 (61%) families presented a monthly income of a minimum wage and owned a home (65%), two families had no income. Fifteen homes presented 4 to 5 residents including the infant, and 19 assessed infants had contact with other children. Mothers were young adults with a mean age of 29 ± 6, with low education (14 presented incomplete primary education); only two mothers were married and five of them had a steady relationship.

The AIMS assessment identified four (15%) infants with a suspected motor development, presenting percentiles below 25%; and only one infant presented no optokinetic nystagmus.

Multivariate analysis showed that the factors which had influenced the development of the four infants who have presented suspected motor development were: not having other children at home ($p = 0.028$, OR = 1.29), not having breastfed until six months of age ($p = 0.011$, OR = 1.69) and low birth weight ($p = 0.06$), Table 02.

Table 2 : Correlation between the groups with and without delay NMD with categorical variables (X2) and numerical variables (Mann Whitney)

Risk Factors	*p*-value	Odds Ratio (IC 95%)
Marital Status	0,32	
Education	0,86	0,83
No of Residents	0,31	
Family Income	0,75	
Other Children	0,028	1,29
E.B.	0,011	1,69
Ocular Movements	0,017	0,75
Type Childbirth	0,73	0,69
Gestational Age	0,40	
Apgar at 1 Minute	2,39	
Apgar at 5 Minutes	0,66	
Birth weight	0,06	
Size at birth (cm)	0,47	
Head Circumference	0,23	

Caption: NMD = normal motor development, No = number; EB = exclusive breastfeeding, cm = centimeters.

IV. Discussion

Although there were no neonatal risk factors, 15% of assessed infants showed some abnormalities of motor development and one infant showed no ocular movements. Moreover, the family dynamics, exclusive breastfeeding until six months, and birth weight influenced the motor ability of infants with suspected development.

The identification of children presenting delays and subtle motor deficits may be a challenge for clinicians and researchers, since the evaluation of infant

motor development may be ineffective when only clinical description is used (Santos, 2008). Motor development is a skill which receives multifactorial influences; this way therapeutic intervention should aim not only biological risks, but also the influence of sociodemographic factors and their relationship with the visual function (Ferreira, 2011).

As for motor response, most infants presented a motor performance within expected levels for the age of six months (mean percentile of 27.46). These data are not similar to Saccani (Saccani, 2013) and Lopes (Lopes, 2004) findings with healthy Brazilian infants, as the values they have found proved to be superior at an average score which was lower to the percentile (Mello, 2004).

By the optokinetic nystagmus movement, we propose in this study an investigation of the oculomotor performance, in an attempt to assess the central processing route and correlate findings between the two instruments. However, this correlation was hampered as only one infant presented abnormal ocular movement; and we believe that motor development and communication skills are impaired in children with visual disabilities, because gestures and social behaviors are learned by visual feedback (Gagliardo, 2004). It is known that not integrating the visual pathway may result in motor impairments (Gagliardo, 2003) (Cassidy, 2000) and our data confirm these findings, since motor development was suspected according to AIMS in only one infant who presented no optokinetic nystagmus.

Previous studies which have assessed motor development in healthy Brazilian infants presented low percentiles; and acquisitions for most tasks occur slowly compared with infants which were assessed in Canadá (Mancini, 2004) (Pilz, 2007) (Santos, 2008). These authors questioned which aspects could justify the presence of the low percentiles presented by Brazilian children and explained that this fact could occur because motor skills acquisition happens in a non-uniform rhythm, is not universal and undergoes cultural changes (Mancini, 2004) (Pilz, 2007) (Santos, 2008).

Although most of the interviewed mothers presented low education level and low income, no correlation was found between these variables and motor development.

This result does not confirm those described in previous studies which have found an association of these variables with socioeconomic status. According to the authors, when income and consumption of goods are low, parents' harmony and the environment well being can be impaired, and may affect the quality of family relationships, as well as disadvantage child development (Saccani, 2009) (Mancini, 2004) (Pilz, 2007). This can be explained by the physical environment limitation, restricting the possibilities for infants' proper exploration and interaction in the environment, thus hampering their global development (Saccani, 2009).

Regarding the fact that low maternal education is a risk factor which causes problems to child growth and development (Pereira, 2011) (Vieira, 2009) (Pilz, 2007), Halpern et al. (Halpern, 2000) found that as maternal education decreases, the risk to present suspect motor development increases; association also mentioned by Moura (Santos, 2008) . In this study, however, despite mothers' low education, these data were not significant.

The monthly family income is crucial to provide families' life quality in accessing health, education, food, housing, among others (Vieira, 2009) (Leone, 2002); and to most survey participants it was lower than the minimum wage, around R$600. Poverty has been considered a constant threat to child welfare, as it promotes limitations to their development opportunities (Zajonz, 2008) (Mancini, 2004). Thus, the lower the family income, the greater children's vulnerability to motor disorders (Halpern, 2000) (Mancini, 2004).

In controversy to the majority of studies, despite of the low family income, it was found that infants presented motor performance considered within normal limits; this can be explained because in low-income homes located in developing countries such as Brazil, the head of the family is usually the one who works, thus the role of child care gets diluted among the several residents of that home. Results show that other 4-5 people also live in 62% of households where assessed children live, including children; 81% of the assessed children lived together with other children. It is believed that early contact with these children has contributed to good motor performance. These data corroborate to Formiga (Vieira, 2009), Magalhães (Magalhães, 2003) and Souza (Souza, 2010) findings. However, the relation between the number of residents in the child's residence and the motor performance is still poorly investigated .

Another point that can be discussed in this perspective is the presence of a stable union between most participants' parents; in his study Formiga (Vieira, 2009), considered this marital status as a potentially protective factor, neutralizing the adversity effect on the child motor development. This author also reported that when parents are in a stable union, family shows greater support for infant care, favoring interactions, emotional balance and proper development.

Breastfeeding can also configure itself as a possible factor which may favor the development; by questioning mothers regarding feeding the infant only with breast milk it was found that 65% of infants have been exclusively breastfed up to six months old. In Zanjonz (Zanjonz, 2008) study it was noted that the longer breastfeeding duration the best assessed children motor performance was, according to his study. Another study found out that children who have never

been breastfed presented a 88% higher chance of having a test resulting in suspected motor development, when compared to those who had exclusive breastfeeding up to six months old (Albuquerque , 2009). The breastfeeding period provides a daily approach, which works as a facilitator of child development. This approach also promotes physical contact with the mother, making it a rich source of stimuli, leading to increased motor stimulation, which triggers appropriate responses for this age group (Zajonz , 2008).

Other studies investigating the influence of birth weight on child development (David, 2012), corroborate to our data (Lima, 2004) (Santos, 2008) (Pilz, 2007), as they demonstrated that the lower the birth weight, the greater the chance of infants to present developmental delay . Although assessed infants are facing social factors that may negatively influence the process of motor skill acquisition, they remain within normal limits. The participants in this study presented an average birth weight of 3459g and gestational age of 40 weeks. The effect of social risk factors on the relationship between biological risk and child development can be understood as a moderating effect. According to Souza & Magalhães (Souza, 2010), since biological factors have great influence on the development in the first year of life, from the second year on, however, it was seen that environmental factors were more relevant (Lima, 2004). Some factors may possibly justify the good development that children presented in this study, although they present no statistically significant relationship; as, for example, the average maternal age of 29 years. To Zajonz (Zajonz, 2008) the higher the maternal age, the better motor performance is shown by children.

There are some limitations in the present study, as the limited sample size and the fact that this is a transversal study. Future researches shall be stimulated using the same population with a more representative sample size, as well as the longitudinal assessment of infant motor development. This study, however, provides important information on infant motor development, demonstrating that even term infants without neonatal risk factors, may exhibit abnormal motor performance and present no optokinetic nystagmus. We note that studies aiming to associate oculomotor development with motor development of children using reliable scales with proven sensitivity and specificity shall be encouraged. Although we do not use a validated visual analogue scale, an object placed in the visual field awakens the child's interest and desire to touch it, stimulating his vision and enhancing ocular movements. These stimuli cause these structures to develop their cell contacts and synapses are realized by neural cells, promoting visual function and making it permanent (Gagliardo, 2003) (Mezzalira, 2005), allowing interaction with the external environment, fostering communication and controlling movements and actions (Pereira, 2011) (Carvalho, 2005) (Costa, 2007) (Mezzalira, 2005) (Bicas, 2003).

These study's practical implications reinforce that knowledge, assessment and the spontaneous observation of visual behavior during the first months of life allows not only to verify how the infant uses his vision to build his sensorimotor universe , but also constitutes a procedure able to detect possible changes in motor and neurological development, for the vision integrates other systems and senses. One of these infants' possible visual apparatus deficits is in their ability to achieve and maintain a normal motor activity. The environmental experiences occurred during the neonatal period influence the neurological maturation, which justifies the proper visual pathways development and motor performance found in our research.

V. Conclusion

Infants without neonatal risk factors may have delayed visual and motor performance, since 15% of our sample presented suspected motor development and one infant showed no optokinetic nystagmus.

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Retrospective Study Evaluating the Management of Psychotic Disorders at Behavioral Medicine Dept – SQUH

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Introduction- Hundreds of millions of people worldwide are affected by mental, behavioral, neurological and substance abuse disorders. For example, estimates made by WHO in 2002 showed that 154 million people globally suffer from depression and 25 million people from schizophrenia. (1) This exerts tremendous social, medical and financial burden. Early intervention and effective management can easily reduce this burden significantly. One other main disorders encountered and constitute real challenge are the psychotic disorders. They constitute 3 to 4 % of all mental disorders (1). They have gained special interest due to its possible chronic course and hence its long term economic and social impact. Cost-effective treatments exist for most disorders and, if correctly applied, could enable most of those affected to become functioning members of society.

GJMR-A Classification : *NLMC Code: WM 90*

Strictly as per the compliance and regulations of:

Retrospective Study Evaluating the Management of Psychotic Disorders at Behavioral Medicine Dept – SQUH

Dr. Amr Guenedi [α] Dr. Yousif Obeid [σ] & Dr. Hanan al Shukri [ρ]

I. Introduction

Hundreds of millions of people worldwide are affected by mental, behavioral, neurological and substance abuse disorders. For example, estimates made by WHO in 2002 showed that 154 million people globally suffer from depression and 25 million people from schizophrenia. (1)

This exerts tremendous social, medical and financial burden. Early intervention and effective management can easily reduce this burden significantly. One other main disorders encountered and constitute real challenge are the psychotic disorders. They constitute 3 to 4 % of all mental disorders (1). They have gained special interest due to its possible chronic course and hence its long term economic and social impact. Cost-effective treatments exist for most disorders and, if correctly applied, could enable most of those affected to become functioning members of society.

II. Objective of our Study

To evaluate our current management of inpatient psychotic disorders at SQUH-Behavioral medicine department.

III. Method

- Data were collected from inpatients computer notes for patients diagnosed with psychotic disorders using the DSM IV criteria (3). No consent was needed since this is a retrospective study and no intervention is done. Patients were chosen according to an inclusion criteria which includes the following:

a) inclusion criteria

- Age group between 18- 65 years old.
- Patients admitted to our psychiatric ward.
- Patients who were followed up for at least 3 months after being discharged from hospital.
- Patients whose diagnosis met the DSM IV criteria for:
  - » Schizophrenia
  - » Schizoaffective disorder,
  - » Depression with psychotic features
  - » Mania with psychotic features
  - » Mixed affective states
  - » Other psychosis

b) exclusion criteria

- Patients who had received ECT or structured psychotherapy
- Patients taking more than one antipsychotic
- Patients taking regular benzodiazepine medications

After data collection we looked at the following:

- Gender
- Diagnosis
- Type of medication
- Average length of stay
- Relapse rate within 3 months of discharge.

IV. Results

According to the collected criteria, the number of patients included in the study was 121 patients. They were 54 males (44.63 %) versus 67 females (55.37 %). The highest age distribution (57 %) was between 20-29 years old. 22.3% were between 30 and 39 years old. 9.1% between 40 and 49, 8.3% between 16 and 19, and 3.3 % over 50 years old (Figure 1).

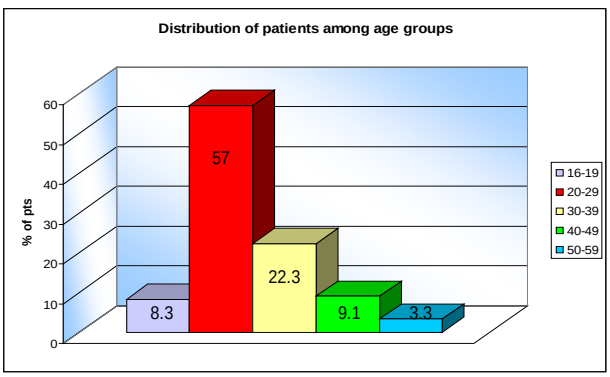

Figure 1 : Showing age distribution

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As per diagnosis it was found the patients with mania were (41.3 %) , Schizoaffective cases were 19.8% positive schizophrenia were 14% ,Unipolar depression with psychotic features were 11.6 % , and those with bipolar depression with psychotic features were 7.5 %. Patients with either mixed affective states (2.5%) or other psychosis (4%) constituted the least percentage among the study group(table 1).

Table 1 : showing percentage of diagnosed cases

Table 1 showing percentage of diagnosed cases	
Disorder	Percentage (%)
Mania	41.3
Schizoaffective	19.8
Schizophrenia (Positive symptoms)	14
Unipolar depression with psychotic features	11.6
Bipolar depression with psychotic features	7.5
Mixed affective state	2.5
Others e.g. Epileptic induced psychosis	4

The average length of stay as per diagnosis reflects the following: 13 days for patients diagnosed as having bipolar depression with psychotic features , 12 days for patients with either a positive schizophrenia or a manic episode, 11 days for pts with the diagnosis of unipolar depression with psychotic features (Figure 2).

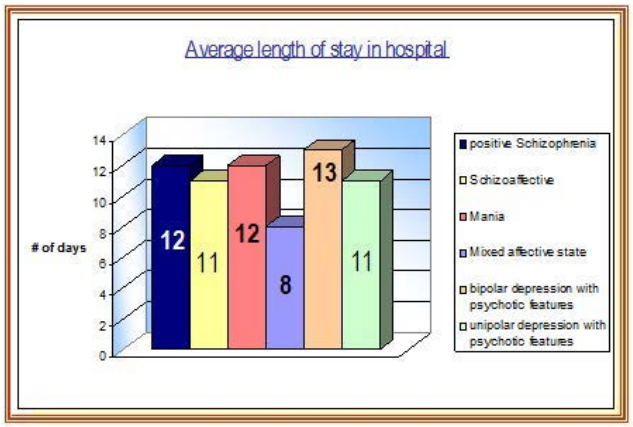

Figure 2

Reviewing our archives and the follow up notes on each visit to the outpatient clinic, we found that 87.61 % of selected patients remained symptom free at least three months after being discharged from hospital. The percentage of patients who relapsed within 3 months after discharge was 12.39 %.9 (Figure 3).

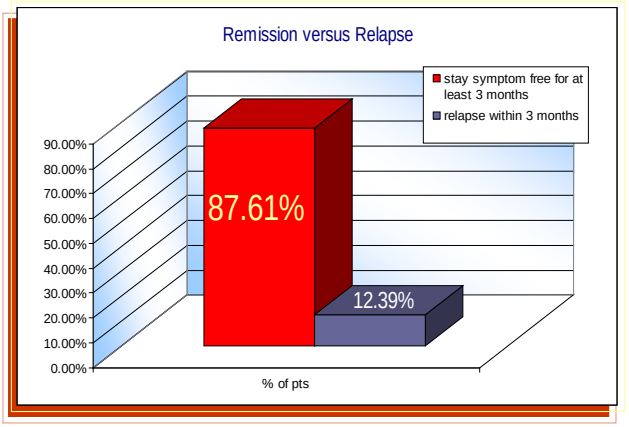

Figure 3

The highest rate of relapse (22.2%) was among patients diagnosed with bipolar depression with psychotic features, followed by those with Unipolar depression with psychotic features (21.4%), schizoaffective disorder (16.6%), positive schizophrenia (11.76%) and finally patients with mania who relapsed within 3 months after discharge were (6 %) of the total percentage of those who relapsed (12.39%).Figure 4.

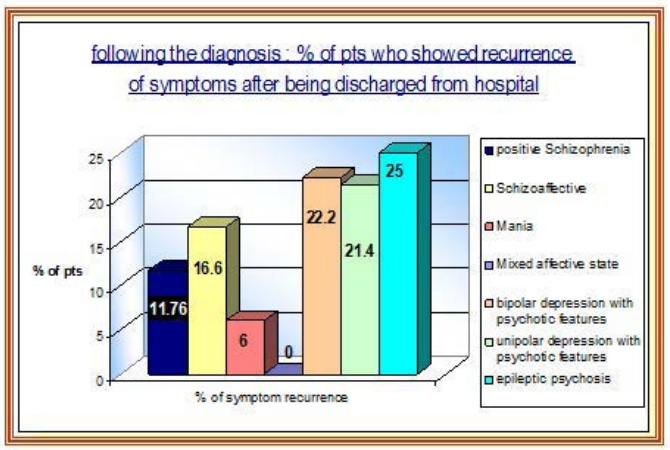

Figure 4

These findings led us to review the antipsychotics we usually prescribe for our patients. We found that three antipsychotics are frequently used: Haloperidol, Risperidone, & Olanzapine. We compared these three medications as regard the field of efficacy.

Figure 5 shows that Haloperidol was the drug prescribed for 37.5 % of those patients diagnosed as having the positive syndrome of schizophrenia and who remained symptom free for at least three months after discharge, compared to 31.2% for Olanzapine, and 6.3 % for Risperidone. According to our findings for such patients, addition of a mood stabilizer or of an antidepressant or both had no remarkable effects.

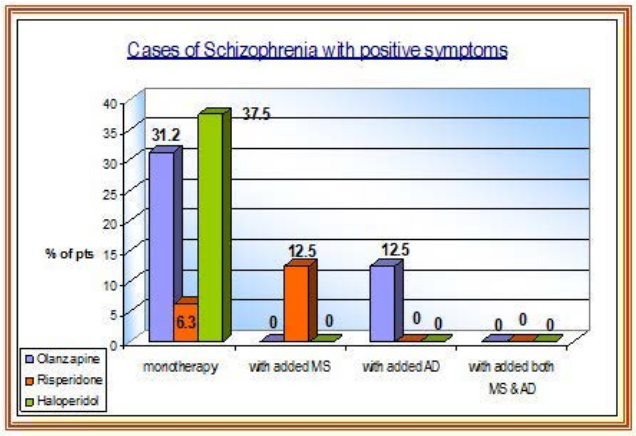

Figure 5

Figure 6 shows that Olanzapine added to a mood stabilizer was the drug prescribed for 45 % of those patients diagnosed as having a schizoaffective disorder and who remained symptom free for at least three months after discharge, compared to 25% for Olanzapine as a monotherapy, and 15 % for Haloperidol combined to a mood stabilizer.

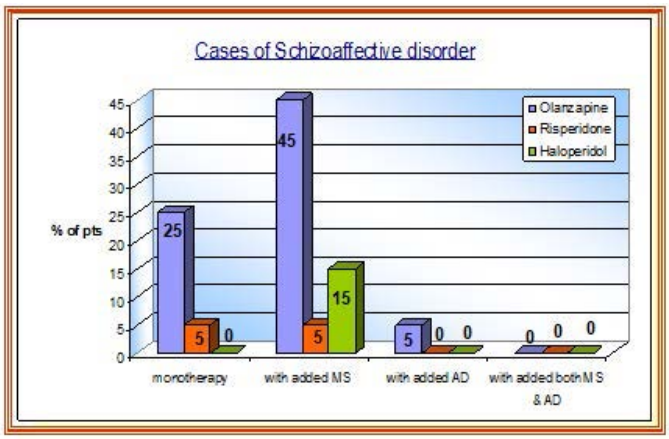

Figure 6

Figure 7 shows that again Olanzapine added to a mood stabilizer was the drug prescribed for 36.17 % of those patients diagnosed as having a manic episode and who remained symptom free for at least three months after discharge, compared to 27.65% for a combination of Haloperidol and a mood stabilizer, and 12.7 % for Risperidone combined to a mood stabilizer. These findings emphasize that mood stabilizers are an essential component in the treatment of acute manic episodes.

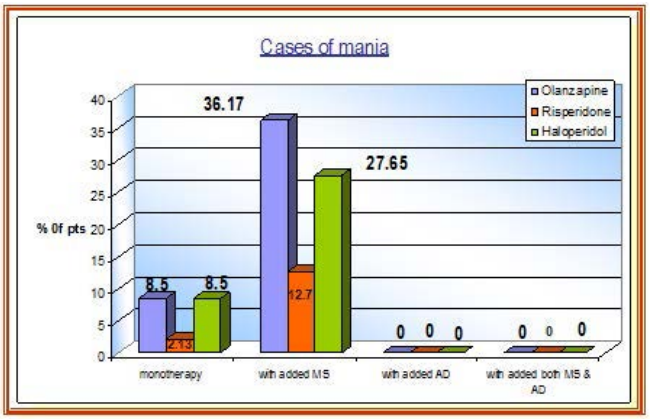

Figure 7

Figure 8 shows that Olanzapine added to a mood stabilizer was the drug prescribed for 44.4 % of those patients diagnosed as having a bipolar depressive disorder with psychotic features and who remained symptom free for at least three months after discharge, compared to 33.3% for Haloperidol combined to a mood stabilizer. And 11.1 % for Risperidone combined to a mood stabilizer.

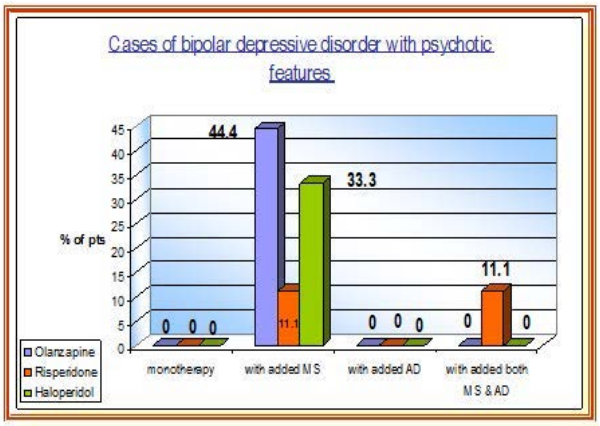

Figure 8

Figure 9 shows that Risperidone added to a mood stabilizer and to an antidepressant was the drug prescribed for 33.3 % of those patients diagnosed as having a unipolar depressive disorder with psychotic features and who remained symptom free for at least three months after discharge, compared to 16.6 % for Risperidone added to antidepressant, 16.6% for Risperidone added to a mood stabilizer, and again 16.6 % for Olanzapine as a monotherapy.

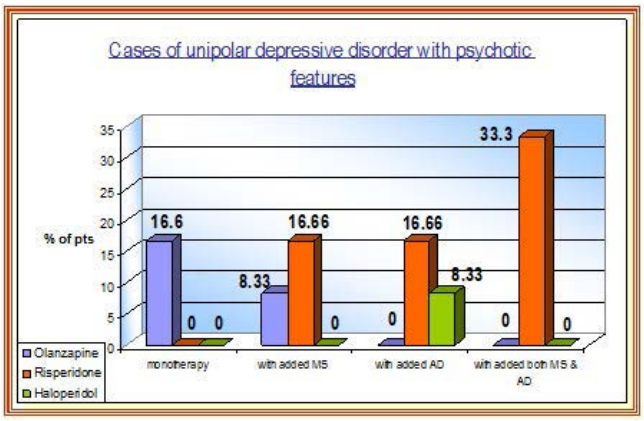

Figure 9

V. Discussion

From the results mentioned above two main findings are to be brought to attention. The first point is the average length of stay as denoted by 11.8days. This is considered to be of great significance if compared with other studies (eg 13 days in the study run by Boronow J) (2). The second point is the low relapse rate in the first 3 months as reflected by the 13% figure, again below much of the reported figures. This is considered to be of great importance since it reflects both short and long term success in management.

Comparing different antipsychotics under study it was found that Haloperidol seems to be the drug of choice in cases of positive schizophrenia. Olanzapine added to a mood stabilizer seems to be the combination of choice in cases of mania, schizoaffective disorders & bipolar depression with psychotic features. Risperidone added to a mood stabilizer and to an antidepressant was found to be the combination of choice in cases of unipolar depression with psychotic features.

VI. Declaration of Interest

The present study was not supported by any pharmaceutical company.

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Electrophysiologically Guided Multitarget Stereotactic Intractable Epilepsy Surgery in Patients with Complex Epileptic Systems

By Sozari A. Chkhenkeli, George S. Lortkipanidze, Tamas N. Rakviashvili, George E. Magalashvili, Eteri Sh. Bregvadze, Alexander Otarashvili & Tamar Sh. Gagoshidze
The University of Chicago, United States

Abstract- *Objective:* The purpose of this study is to achieve beneficial treatment outcomes for severe intractable epilepsy patients using neurophysiologically guided stereotactic multitarget surgery.

Material and methods: Ninety-three patients (64 men, mean age 25 y (SD – 11 y, range 6-57 y), mean duration of illness 18 y (range 3-36 y) underwent multitarget stereotactic cryosurgery guided by pre- and intraoperative depth electrode (stereoelectroencephalography – SEEG) evaluation. Multiple unilateral and bilateral amygdalatomies, partial anterior and total hippocampotomies, cingulotomies, fornicotomies, CM and DM thalamotomies, postero-medial hypothalamic, Forel-H-tomies, and fasciculus uncinatus lesions in individual combinations were performed according to SEEG findings.

Keywords: *complex epileptic systems, intractable epilepsy, neurophysiologic guidance, psycho-emotional disturbances, stereotactic multitarget epilepsy surgery.*

GJMR-A Classification : *NLMC Code: WL 370, WL 385*

Strictly as per the compliance and regulations of:

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Abstract- Objective: The purpose of this study is to achieve beneficial treatment outcomes for severe intractable epilepsy patients using neurophysiologically guided stereotactic multitarget surgery.

Material and methods: _ Ninety-three patients (64 men, mean age 25 y (SD – 11 y, range 6-57 y), mean duration of illness 18 y (range 3-36 y) underwent multitarget stereotactic cryosurgery guided by pre- and intraoperative depth electrode (stereoelectroencephalography – SEEG) evaluation. Multiple unilateral and bilateral amygdalatomies, partial anterior and total hippocampotomies, cingulotomies, fornicotomies, CM and DM thalamotomies, postero-medial hypothalamic, Forel-H-tomies, and fasciculus uncinatus lesions in individual combinations were performed according to SEEG findings.

Results: The SEEG studies revealed the existence of complexly organized multistructural epileptic systems in cases of long-standing severe intractable epilepsy. Engel's (1993) Class I outcome was achieved in 51%, worthwhile improvement (Classes II-III) was observed in 28% and no worthwhile improvement (Class IV) was observed in 21% of all patients. Remarkable normalization of the psycho-emotional state was achieved for patients with pre-surgical behavioral problems. No seizure, or cognitive, or memory states worsening was observed in this cohort of patients. The follow-up for seizures and behavioral abnormalities was up to10 years.

Conclusion: Multitarget electrophysiologically guided stereotactic surgery can have a beneficial effect on seizure frequency and severity, and normalize psycho-emotional state and behavior in long-standing intractable epilepsy patients. We did not postsurgical decline in cognitive domain of our patients, and the benefits of seizure control using this technique, im our opinion,outweigh possible risk of cognitive decline.

Keywords: complex epileptic systems, intractable epilepsy, neurophysiologic guidance, psycho-emotional disturbances, stereotactic multitarget epilepsy surgery.

I. Introduction

According to widely accepted criteria, the potential candidates for resective intractable epilepsy surgery should have a detectable epileptic focus localized outside of the eloquent cortical areas and, in cases of temporal lobe epilepsy, within one temporal lobe. Adherence to these criteria leaves no hope for a large group of disabled patient with severe intractable epilepsy and epilepsy-induced psycho-emotional disturbances, and limits the cohort of potential candidates for successful epilepsy surgery. A multicenter study [1] demonstrated that 30% of patients who underwent presurgical evaluations for resective epilepsy surgery ultimately did not have surgery because of multifocality of seizures, localization of epileptic focus (foci) within eloquent cortical areas, or the risk of severe postsurgical memory impairment. For these patients, leaving seizures uncontrolled may result in further decline of speech, memory, learning, emotional stability, or cognitive and psychosocial dysfunction, leading to dependent behavior and a restricted lifestyle.

However, localization or approachability of an epileptic focus is not the only limitation. Contemporary epilepsy surgery is directed mainly against a solitary epileptic focus whereas intractable epilepsy may be considered as a dynamic multifactoral process with complexly and multistructurally organized epileptic networks [2-15]. Conventional resection of most active elements of these epileptic networks is hard to perform, but stereotactic method offers a possibility to conduct simultaneous surgery on the key elements of epileptic network. The outcomes of the previous stereotactic surgeries with small lesions targeted also to the sole epileptic focus or neural pathway were not found to be as favorable as those obtained with standard temporal resections [16]. To summarize the existing experience with stereotactic lesional treatment of epilepsy, it is necessary to understand that there are particular reasons that lead to the failure of stereotactic method for epilepsy treatment. In many clinics, these surgeries have been performed using "standardized" operations, without detailed detection of the "architecture" of the pathologic intracerebral network (epileptic system), without detailed neurophysiological analysis of the interrelations between key elements of these epileptic systems, and without modification of surgeries according the needs of each individual patient.

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Furthermore, it could be that not all key elements of the epileptic system were lesion allowing the remaining parts to transform and continue their activity if left intact. Our experience suggests neurophysio;ogically guided precise stereotactic surgery, which impacts key multitarget elements of the epileptic systems, may frequently lead tp reorganization and normalization of the brain activity resulting in successful clinical outcomes.

II. Patients and Methods

a) *Patients*

This study included a highly selected cohort of 93 long-standing intractable epilepsy patients (64 men, mean age 25 y (SD- 11 y, range 6-57 y), mean duration of illness 18 y (SD- 9.63, range 3-36 y), and the frequency of seizures occurrence ranged from 6 to 70 per month. Most of these patients were clinically defined as intractable temporal lobe epilepsy patients with a likelihood of complexly organized epileptic systems, including limbic-thalamic structures. Seizure manifestations included complex partial seizures with and without secondary tonic-clonic generalization, "primary" generalized seizures with elements of psychomotor seizures. Most of the patients were additionally incapacitated by psycho-emotional and behavioral disturbances (Tables 1 and 2). Multiple presurgical scalp EEGs, long-term video-EEG monitoring and telemetric EEG recordings revealed bitemporal and multifocal independent, as well as bilateral synchronized interictal and ictal epileptiform abnormalities (Table 3).

Table 1 : Clinical manifestations of seizures

Types of epileptic seizures*	Number of patients
Complex partial seizures (CPS) with frequent secondary fast or delayed generalization	42
Clinically "primarily" generalized seizures with "postictal" automatisms	34
CPS or "primarily" generalized seizures with postictal lateralizing neurological deficit	31
CPS with postictal twilight states	23
Clinically "primarily" generalized seizures with elements of partial motor seizures	19
Drop-attacks-like seizures with subsequent tonic stiffening	17

** Types of seizures are described not just according to Classification but with important clinical and behavioral phenomenology. Most of patients exhibited more than one type of seizures.*

Table 2 : The main clinical manifestations of the psycho-emotional and behavioral disturbances

Types of the psycho-emotional and behavioral manifestations*	Number of patients
Interictal chronic depression	43
Interictal hypersexuality**	13
Interictal acute psychotic states concomitant with "forced normalization " of EEG	11
Interictal emotional excitement, anxiety	23
Preictal changes of mood, irritability, fear, explosiveness, and anxiety	52
Postictal fear and/or anxiety	14
Postictal psychotic states, anger attacks, excessive hypersexual behavior	12

** Table 3 mirrors the main types of the psycho-emotional and behavioral manifestations. Many of patients demonstrated more than one pattern of an abnormal psycho-emotional state and frequent transformation of one psycho-emotional state into another.*

*** We do not describe hyposexuality, which is common for temporal lobe epilepsy and less disturbing to everyday life.*

Table 3 : EEG characteristics of the scalp video-EEGs or telemetrically captured seizures

EEG patterns of seizures*	Number of patients
Temporal unilateral with or without generalization	13
Temporal unilateral → contralateral temporal mostly with generalization	22
Temporal unilateral → contralateral fronto-parietal with or without generalization	13
Bitemporal independent with or without generalization	25
Bitemporal bilaterally synchronous mostly with instantaneous generalization	8
Temporal unilateral → ipsilateral frontal → contralateral frontal with generalization	11
Temporal unilateral → bilateral frontal with generalization	7

Multifocal (mostly anterior frontal or posterior temporal) with generalization	14
"Forced normalization " of EEG with "primary" generalized seizures**	10
Temporal lobe electrodecremental event → temporal ipsilateral with generalization	31
Diffuse electrodecremental event with "primary" generalization	27

** This Table presents the main electrographic abnormalities, which were dominant in the recorded interictal and ictal EEGs. Arrows indicate a direction of seizure spread detectable in the EEG and chronic SEEG.*
*** Forced normalization of EEG could be observed in patients with focal temporal epileptic focus on EEG, bitemporal abnormalities, as well as, in patients with multifocal and diffuse epileptiform activity.*

The patients we have studied have been divided into two groups, A and B, different from each other by the degree of neurophysiologic analysis of the clinico-EEG/SEEG data and by the number and volume of stereotactic lesions. Group A included 31 patients (39 surgeries) whose EEG/SEEG data were assessed only from the point of view of localization of the putative epileptic focus. In this group, the goal of the patient's evaluation was to detect a restricted epileptic focus, supposedly responsible for the full clinical set of symptoms, and stereotactic lesions were limited in number and the size of the lesion according to existing surgical practices.

Group B consisted of 76 patients (62 patients + 14 patients from Group A with unsatisfactory surgical outcome who underwent reoperation) included in Group B were operated on using multitarget electrophysiologically guided lesioning of the key elements of the individually organized epileptic systems. The extent of surgery was planned according to the results of the pre- and intrasurgical investigation in each particular patient. The age, clinical, electrophysiological, CT, MRI, and neuro-psychological status of patients in Group A and Group B were similar, and their treatment outcomes were comparable.

b) Pre-surgical evaluation

As a rule, AEDs were temporary reduced, and at least two spontaneous seizures documented by long-term video/EEG, video/telemetric EEG/SEEG monitoring were required during the pre-surgical evaluation. In the assessment of the patients psychoemotional state, attention was focused on the interictal, immediately preictal and postictal manifestations. The neuro-psychological battery included the adapted Wechsler (WAIS & WISC) Scales, TAT, MMPI and Rorschach tests. Patients' evaluations revealed different degrees of the temporo-limbic system involvement with putative lateralization in some cases Most patients had an IQ ranging from low-average to average, exhibited both verbal and nonverbal memory difficulties, indicating bitemporal dysfunction, and displayed interictal psychotic profiles on the MMPI. To assess memory, we selected a number of the most frequently occurring common nouns, paying particular attention to their length (max. 2-4 syllables). In the memory examination, during the one tesr the patient was presented with series of ten words and a short (5-6 word) sentence presented verbally twice. The second test included ten word lists and series of material that cannot verbalized readily, such as places, unfamiliar faces, or abstract designs and drawings presented visually for one minute. Memory assessment was based on the ability of patients to reproduce presented material after five minutes.

c) Decision making

The results of neurologic, EEG, CT, and MRI evaluations in this cohort of patients, especially in the Group B patients, were inconclusive about the site of seizure origin. The results of the assessment of clinico-neurophysiologic data, including neuro-psychological assessments, served as the basis for an elaboration of the preoperative hypotheses about the organization of the putative individually organized epileptic system and indications for invasive SEEG-evaluations for the detection of the key elements of these systems. Concurring with the statement that a proposed operation for an epileptic patient cannot be safely based on a general hypothesis, and should only rest on knowledge of the functional organization of the epileptic system, we did not make standardized preoperative decisions about the extent of surgery. The final decision about the lesioning of specific brain structures involved in the individual epileptic system was made during surgery, and was based on the cumulative assessment of the pre- and intrasurgically obtained information.

III. Surgery

a) Surgery, methods

Stereotactic operations were performed using Talairach's stereotactic frame. Electrode insertion was usually performed under local and neurolept anesthesia with N_2O + O_2 ventilation. Subsequent intrasurgical diagnostic studies and lesions were performed in extubated awake patients receiving local anesthesia. Temporal lobe mesiobasal structures were located using an axis of reference constructed on the temporal horn fiducially points [17]. Amygdala and hippocampal structures and exact locations of the intracerebral electrodes were defined by intrasurgical orthogonal televentriculography using water-soluble contrast

agents. Thalamic, subthalamic, and hypothalamic structures were reached by coordinates related to AC-PC line, saggittal midline, and a proportional grid according to thalamic size. The SEEG electrodes and lesional tools for evaluation/lesion of the thalamo/subthalamic structures were usually inserted using tangential approach. The cingular, fornical, anterior commissure, and temporal lobe instruments were usually inserted through a lateral approach [17].

b) Surgery, targeting

Hippocampus. In several cases, we used a posterior longitudinal approach to the hippocampus, but our study demonstrated that this approach does not always allows to reach a whole hippocampal volume using just two fiducially points: entry point and uncus [18]. That is the reason why we prefer the lateral approach to different parts of hippocampus. For a "total" hippocampotomy on the side of putative dominant epileptic focus, we usually performed three lesions of different volume, intending to maximally include the intraventricular part of structure as corresponding to the CA1-CA3 fields of the cornu Ammonis [19]. The epileptic focus activity recorded by each SEEG electrode's five contacts determined the volume of the lesion. Anterior hippocampotomy was limited to the head of hippocampus, including its intraventricular part, the digitationes hippocampi, and an extraventricular or uncal part primarily targeted on the inferior and medial part of CA1 (Sommer) sector as most vulnerable part of hippocampus. The CA1 sector of hippocampus is a source of hippocampo-cortical output to the prefrontal and orbito-frontal cortex [20, 21] and appears to be an important target for surgery.

Fornicotomy. Pursuing the goal to perform total hippocampotomy (stereotactic "hippocampectomy"), we usually performed a fornicotomy ipsilateral to the subtotal hippocampotomy in the compact part of the fornical columns at the level of anterior commissure to prevent the possible spread of epileptic activity from the remaining posterior part of hippocampus to the mamillary body, thalamus, and cortex.

Amygdala. A total amygdalatomy was usually performed in isolation, or on the side of dominant epileptic focus and total hippocampotomy. Contralateral amygdalatomy, when it was performed, was usually centered on its basal, lateral, and central nuclei which have limbic function and output to the dorsomedial thalamic nucleus, and then to the prefrontal cortex, as well as to the lateral hypothalamus and tegmental area. The right amygdalatomy usually was performed slightly larger than left, because of the interhemispheric asymmetry of human amygdalas [22, 23].

Cingulum. Anterior cingular cortex (field 24 of Brodman) and cingulum bundle. Cingulotomies were performed to remove both anterior cingulate cortex and the cingular bundle in cases with apparent involvement of anterior cingular area in seizure spread. Intraoperative cerebral angiography was used for the precise targeting of the limbic part of the gyrus cunguli located between callosal and calloso-marginal sulci and for preventing hemorrhagic complications. Calloso-marginal sulcus is often doubled, and more frequently, it is doubled in the right hemisphere. In such cases, the specifically limbic cortex is limited to the internal segment of gyrus. The secondary branches of the A2 segment of the anterior cerebral artery very well outline these anatomical peculiarities. Beside that, the diameter of the left A2 is bigger, and the difference in diameters can be about 0.2-5.0 mm. The intraoperative angiography allows the precise targeting of the limbic cortex, as well as avoiding hemorrhagic complications [24]. Special attention was given to the lesion extent in the coronal plane, because it has been stated that sometimes the lesion might not involve the cingulum bundle [25].

Forel-H- fields. Campotomy. Campotomy was performed in the cases of fast frontal and prefrontal seizure spread and motor generalization to intercept the descending impulses and elevate the threshold of motor structures in order to reduce or avoid the clinical tonic-clonic seizure component [26]. The Forel-H- fields was targeted in cases with apparent involvement of this area in seizure spread and was centered on the prerubral area, aiming at the H3 field uniting H1, H2 fields and zona incerta, which receives prefrontal motor afferents. Cryogenic lesions in this area never exceed 4mm in diameter.

Postero-medial hypothalamotomy. Postero-medial hypothalamotomy was performed in patients with seizure-related aggressive behavior and hypersexual abnormalities, and SEEG verification of hypothalamic involvement into the seizure discharge propagation. The 4-5 mm diameter target was chosen according to Sano [27] and was located 1 mm anterior and 3-4 mm inferior to the CA-CP line midpoint, 1-3 mm lateral to the wall of third ventricle.

The fornicotomies, cingulotomies, Forel-H-tomies, and postero-medial hypothalamotomies were performed not as single-target epilepsy surgeries as it was introduced by their authors, but as lesions of important epileptic system parts performed simultaneously with lesion of dominant epileptic focus (foci).

c) Surgery, SEEG evaluation, functional probes

Intracerebral electrodes for chronic and intrasurgical SEEG evaluations and functional probes with direct stimulation, local polarization and cooling of deep brain structures were described earlier [28]. EEG/SEEG recordings (DC-80 Hz bandpass) were obtained with a 20-channel Alvar recording system (Alvar-Electronic, France). Local diagnostic bipolar stimulations (usually 0.5-5.0 mA, 0.1-0.2 ms, 0.5-1.0 s)

were performed using Nihon-Kohden (Tokyo, Japan) stimulators and constant-current square pulses of alternate polarity with parameters chosen to avoid tissue damage [29]. The pharmacological provocation and augmentation of focal epileptic activity was achieved with i.v. administration of 50 -100 mg Brevital (Metohexital) and 25 mg/20 s Bemegride (Megimide) until the emanation of epileptic focus activity [30].

The temporary reversible "shut-off" of deep brain structures was achieved with local reversible cooling and/or local low-intensity (0.5-1.0 mA) anodic polarizations. This allowed us to evaluate the interrelations of the epileptic system elements and avoid the postsurgical activation of the previously less active brain structures after lesion of the dominant focus [3, 28, 31].

The intraoperative study protocol consequently included: 1) recording of interictal electrical activity, spontaneous focal subclinical and spreading epileptic activity; 2) diagnostic electrostimulation of the elements of putative epileptic system; 3) reversible "shut-off" of active elements of these systems; 4) pharmacological augmentation and provocation of epileptic activity and discharges. Each next step in this protocol was performed 5-10 min after returning the SEEG/EEG activity to the baseline. To prevent clinical seizures, 10 mg Valium was usually administered to the patient after the final pharmacological stage of study.

During independent assessment (SCh, GL, and ShB) of the SEEG/EEG data, the most important patterns were: 1) absence of spontaneous epileptic activity; 2) focal intermittent epileptic activity or discharges in one of the recorded structures; 3) spread of this epileptic activity to brain structures of same anatomical/functional level (i.e. amygdalar activity to the hippocampus and *vice versa*); 4) spread of epileptic activity beyond the lobar limits of one hemisphere (i.e. spread of amygdala-hippocampal activity to the homolateral frontal lobe); 5) involvement of symmetrical contralateral structures; 6) spread of deep brain activity to the contralateral scalp EEG; 7) the sequence of discharge spread and generalization; 8) temporary focal suppression of activity in one of brain structures during a focal subclinical seizure in another, or augmentation of epileptic activity during the temporary "shut-off" of an epileptic focus.

d) Surgery, lesioning

The electrophysiological criteria for lesioning were:

a) prevalence of interictal activity from one side, obvious and reiterative following changes in interictal activity in one temporal lobe to changes in the temporal lobe with a prevalence of spike activity;
b) stable onset of subclinical and clinical seizures from the same temporal lobe;
c) stereotyped initial clinical manifestation of seizures;
d) apparent unilateral CT, MRI, and positive ventriculography changes. Additionally, the mutually suppressive interactions of hippocampal epileptic foci heralding possible activation of another hippocampal epileptic focus after the ablation of one of them [28] served as an indication for bilateral hippocampal surgery. Cryolesions (freezing) of the epileptic foci tissue were performed using a portable cryosurgical device producing precisely calibrated and volume-controlled lesions [32].

e) Post-operative evaluation and follow-up

Postoperatively, the EEG and neuropsychological status of all patients were evaluated twice during their two-week hospital stay; 87 patients were evaluated in 3 and 6 m, 78 - after one year, 53- after two years, 31- after five years, and 17 patients after 10 years of surgery. Additional multiple EEG evaluations were performed in between these established times. Postsurgical changes in intellectual, memory, and language were additionally assessed based on self-reports, as well on the reports of family members.

All 93 patients were evaluated and operated on at the Center of Functional Neurosurgery and Epilepsy Surgery of *The Institute of Clinical and Experimental Neurology*, (Tbilisi, Georgia).

The experimental protocol was approved by the Institutional Medical Council (an analogy of the Institutional Review Board) with written informed consent being obtained from all patients or their guardians.

IV. Results

The outcomes of surgery in Group A patients were in general not as good as expected. The exception was a considerably better outcome in five patients who received an additional stereotactic amygdalatomy with partial anterior hippocampotomy contralateral to the previous unsuccessful anterior temporal lobectomy because of activation of the contralateral temporal lobe epileptic focus after their first surgery (Table 4).

Table 4 : Types of surgeries performed for Group A patients and their outcomes with respect to seizures (follow-up 1-5 years)

Types of Surgery		Side of surgery		Outcomes of surgery												
		R	L	Class I				Class II				Class III		Class IV		
				A	B	C	D	A	B	C	D	A	B	A	B	C
1. Unilateral VL-thalamotomy		2	1	-	-	-	-	-	-	-	-	-	-	-	3	-
2. Unilateral amygdalatomy		1	3	-	-	-	-	-	-	-	-	-	-	1	3	-
3. Bilateral amygdalatomy		6	6	-	-	-	-	1	2	1	-	-	-	1	1	-
4. Consecutive unilateral amygdalatomy + ant. hippocampotomy*		1	2	-	-	-	-	-	-	-	-	-	2	1	-	-
5. Unilateral amygdalatomy + hippocampotomy		7	3	-	-	1	-	-	2	-	-	4	-	3	-	-
6. Unilateral amygdalatomy + ant. hippocampotomy**		3	2	2	1	-	-	-	-	-	-	2	-	-	-	-
Total	lesions	20	17													
	patients			2	1	1	-	1	4	1	-	6	2	6	7	-

** The interval between consecutive unilateral surgeries was 8 months.*

*** These five patients received stereotactic amygdale-hippocampal surgery after an unsuccessful anterior temporal lobectomy and postsurgical activation of the contralateral epileptic focus. The interval between consecutive surgeries was approximately one year.*

Meticulous analysis of the already performed surgeries results and growing clinical and SEEG data revealed the complicated interrelations between the ipsi- and contralateral brain structures, and variable paths of seizure spread and generalization in our cohort of patients.

Accordingly, our goals for patients' evaluation and surgery were expanded. The pre- and intraoperative evaluation goal appeared as detection of the most active elements of the epileptic system, evaluation of the variants of their interrelations and pathways, and the consequence of epileptic discharge spread in each individual patient. The deep electrode studies revealed the different variants of architecture of the epileptic systems and spread of epileptic discharges in intractable epilepsy, which influenced the surgical strategy and outcome. First, it was found, at least in our cohort of patients, the almost constant bilateral involvement of amygdala-hippocampal complexes in the epileptic process. A strictly unilateral mesiobasal epileptic focus was found in 17% (16/93) of cases. For the remaining 77 patients, seemingly bilateral interictal and ictal epileptic activity was assessed as predominantly unilateral in 19% (18/93) of cases. In all other cases (59/93, 64%), the interictal as well as spontaneous ictal epileptic activity revealed the bilateral, mostly independent seizure onset and involvement of temporal lobe mesiobasal structures in the epileptic process. The degree of this involvement differed, including continuous or intermitted interictal epileptic activity in both hippocampi, spontaneous subclinical seizures in the one amygdala-hippocampal complex and persistent interictal epileptic activity in the contralateral structure with the involvement of ipsilateral amygdala (Figure 1, A), and without amygdalar participation (Figure 1, B). It is notable that the fornical activity in Figure 1 (A) remained unchanged during continuous epileptiform activity in the right hippocampus, and suggested a relatively lower potential of right hippocampus to trigger a spreading and generalizing seizure. However, the absence of the right fornix participation in this spread suggests the propagation of epileptic discharge through fasciculus uncinatus. Hippocampal and amygdala-hippocampal seizures may develop in both temporal lobes independently, as well as simultaneously with clinical manifestations of psychomotor seizures without convulsive generalization and obvious scalp EEG changes. These different variants of seizure spread were reflected in different EEG and clinical manifestations of seizures observed in the same patient.

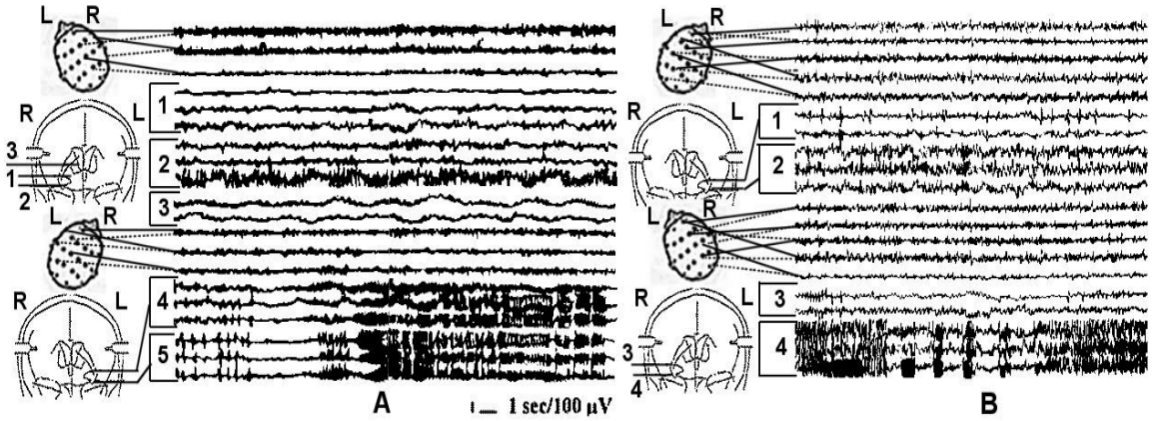


Figure 1

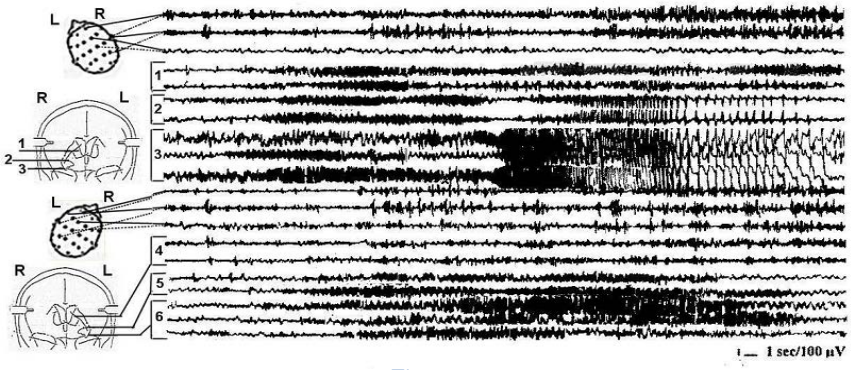
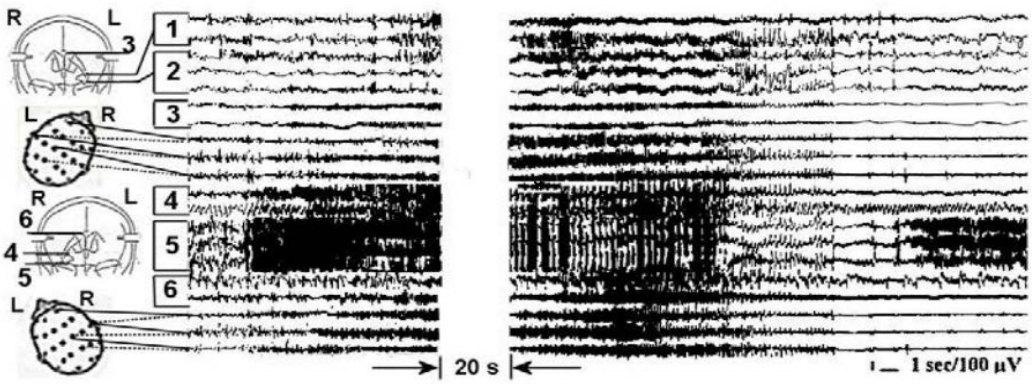


Figure 2

Figure 2 depicts the right focal mesiobasal seizure onset with its spread and generalization presumably through the right fornix and with preferential right cortical involvement. The involvement of the contaralateral mesiobasal structures developed later. This type of bitemporal epilepsy with secondary generalization primarily through the side of initial seizure onset is an example of when surgery might be limited to unilateral amygdala-hippocampotomy and fornicotomy, despite the involvement of contralateral mesiobasal structures.

Figure 3 depicts the bilateral spread of a right mesiobasal epileptic seizure with bilateral cingular and cortical involvement and subsequent generalization in a patient with depression and anxiety. The contralateral amygdala-hippocampal involvement develops after cortical generalization indicating a presumed secondary fronto-temporal seizure spread into the left amygdala-hippocampal complex. Additional right hippocampal focal subclinical discharge developed immediately after the cessation of a generalized seizure, emphasizing a heightened epileptogenicity of that structure, and confirmed the need of total hippocampal ablation in this patient. This case could have been also an example of unilateral right amydgala-hippocampectomy, but because of his depression and anxiety, the bilateral amygdalatomy and right hippocampotomy with bilateral cingulotomy was performed. The additional bilateral cingulotomy was performed because of the active cingular participation in the seizure propagation, in addition to severe depression and anxiety in this particular patient.



Figures 3

In our cohort of patients, we did not observe initiation of seizures at the diencephalic level. Focal hippocampal seizures may spread to the contralateral hippocampus, and bilaterally over the cortex and generalize without involvement of the anterior thalamic nuclear complex or nucleus Centrum medianum (CM). However, the involvement of thalamic CM nucleus into seizure propagation and generalization may occur through different mechanisms of seizure spread and "maintenance" (Figure 4, A and B). Figure 4 (A) depicts a left hippocampal seizure spreading contralaterally and into the fornix with generalization and continuous involvement of CM and cortex. Part B of Figure 4 pictures a secondary generalized seizure involving CM and continuing in the CM and cortex after the seizure in the initiating epileptic focus in the right amygdala-hippocampal complex had ceased. In the first case (Figure 4, A), CM may play a passive role of just "passing" the seizure through the thalamus, whereas in the second case (Figure 4, B), the non-specific thalamic CM nucleus is included in the thalamo-cortical reverberating circuit synchronizing epileptic activity at this level and maintaining a generalized seizure after the focal seizure initiating discharge had ended.

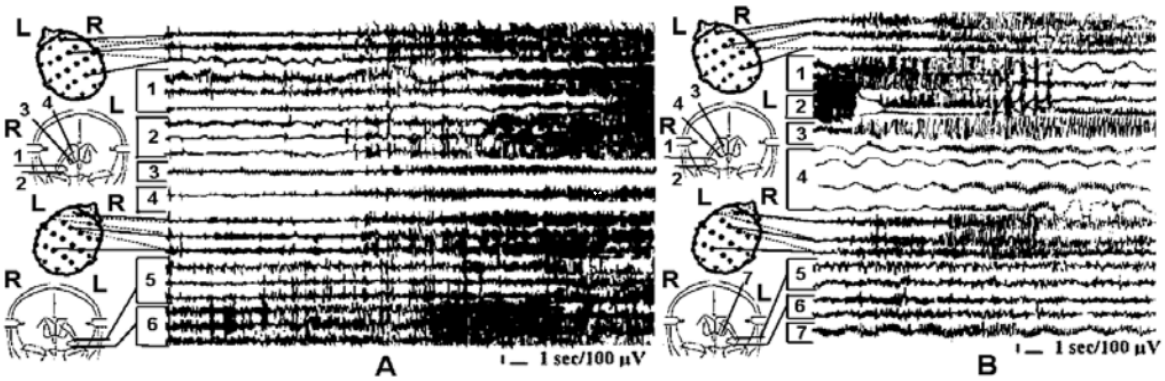


Figure 4

In patients with epilepsy and concurrent psycho-emotional disturbances, a fast involvement of the thalamic dorso-medial (DM) nucleus and postero-medial hypothalamus (PMH) in their generalized seizures originating from temporal lobe mesiobasal structures was frequently observed. Figure 5 presents the chronic SEEG of a patient with frequent secondary generalized complex partial seizures, interictal emotional instability, fear auras and frequent postictal twilight states with sexual aggression. It is notable that hypothalamo-thalamic entrainment develops prior to the contralateral deep and cortical spread of the initially unilateral deep temporal lobe discharge. This preferential spread of epileptic discharge might cause the specific clinical manifestations in this particular patient.

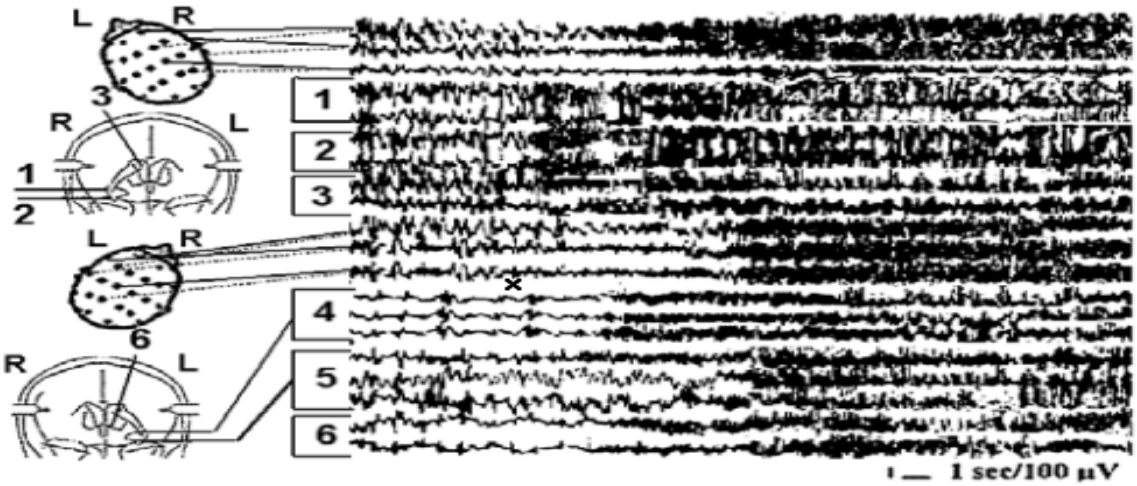


Figure 5

The types of surgeries performed for patients in Group B on the basis of detailed cliniconeuro-physiologic analysis of each individual case, and outcomes of these surgeries for seizures are presented in Table 5. For Group B patients, we performed 17 unilateral amygdala-hippocampotomies, 38 bilateral amygdalatomies with unilateral hippocampotomies, 21 bilateral amygdalatomies and unilateral hippocam-

potomies in combination with contralateral anterior hippocampotomies. The other extratemporal lesions combined with the temporal lobe mesiobasal targets were performed based on the meticulous assessment of all evaluation data.

Table 5 : Types of surgeries performed for Group B patients and their outcomes with respect to seizures (follow-up 1-5 years). Numbers in parentheses represent the Group A patients received reoperation

Types of Surgery	Side of Surgery[1]		Results of surgery												
	R	L	Class I				Class II				Class III		Class IV		
			A	B	C	D	A	B	C	D	A*	B	A	B	C
1. Bilateral amygdalatomy + hippocampotomy	7 4	7 3	1(2)	-	3	-	-	-	-	-	1	-	-	-	-
2. Bilateral amygdalatomy + hippocampotomy + fornicotomy	12 8 3	12 4 9	2(1)	2(1)	-	-	1	-	-	-	2	-	2	1	-
3. Bilateral amygdalatomy + hippocampotomy + bilateral Forel-H-tomy	5 2 5	5 3 5	-	2	1	-	-	-	-	-	-	-	1	1	-
4. Bilateral amygdalatomy + hippocampotomy + fornicotomy + Forel's H-tomy	8 5 - 4	8 3 4 1	1	-	2(3)	-	-	-	-	-	2	-		-	-
5. Bilateral amygdalatomy + hippocampotomy + cingulotomy + fasc. uncinatotomy	6 4 4 1	6 2 2 4	-	-	1	-	2	-	-	-	1	-	1	1	-
6. Bilateral amygdalatony + hippocampotomy + ant. hippocampotomy + bilateral cingulotomy**	5 2 2 5	5 3 3 5	-	-	1	-	1	1	1	-	-	-	-	1	-
7. Bilateral amygdalatomy + hippocampotomy + ant. hippocampotomy + DM-thalamotomy	9 6 6 1	9 3 3 1	2(1)	-	1(2)	-	-	1	-	(1)	-	-	1	-	-
8. Bilateral amygdalatomy + hippocampotomy + ant. hippocampotomy + CM-thalamotomy	7 5 5 3	7 2 2 2	2(1)	1	-	-	-	1	-	-	-	-	1	1	-
9. Unilateral AHT*** + CM-thalamotomy + fornicotomy	4 2 1	2 3 5	1(1)	-	-	-	1	-	-	-	1	1	1	-	-
10. Unilateral AHT + CM-thalamotomy + Forel-H-tomy	5 4 4	3 2 3-	1	-	1(1)	-	-	-	2	-	-	-	2	1	-
11. Unilateral AHT + DM-thalamotomy + PMH**** + fasc. uncinatotomy	1 1 - 2	2 2 3 1	-	1	-	-	1	-	-	-	-	-	-	1	-
Total patients			10(6)	6(1)	10(6)	-	6	3	3	1	7	1	9	7	-

[1] The numbers in these columns represent number of lesioned structure, not the number of patients.
** Worthwhile improvement means 50 -75% reduction of seizure frequency.*
*** Cingulotomy means anterior cingular cortex and cingular bundle lesion.*
**** AHT stands for ipsilateral amygdalatomy and subtotal hippocampotomy*
***** PMH means postero-medial hypothalamotomy.*

The 39/76 patients of Class I outcome composed 51% of patients comprising Group B. Worthwhile improvement (Class I-III) was obtained for 60/76 (79%) patients, and no worthwhile improvement (Class IV) was observed for 16/76 (21%) of patients. Within Class IV results, 9/16 patients had a significant

reduction of seizures (Class IV, A). No seizure worsening was observed for this cohort of patients. The relapse of seizures in patients with Class I-III outcomes was observed in seven patients (12%). None of these cases became intractable again. A comparison of outcomes with respect to seizures for Group A and Group B (Table 6) demonstrates considerably better results for Group B, especially in Engel's Classes I and II (free of seizures and rare seizures).

Table 6 : The comparison of the surgery outcomes with respect to seizures for patients of Croups A and B (follow-up1-5 years)

Classes of outcome*	Group A	Group B
Class I Free of disabling seizures**	4 (13%)	39 (51%)
Class II Rare disabling seizures***	6 (19%)	13 (17%)
Class III Worthwhile improvement****	8 (26%)	8 (11%)
Class IV No worthwhile improvement	13 (42%)	16 (21%)
Total	31 (100%)	76 (100%)

** According Engel et al. (1993).*
*** Excluding early postoperative seizures.*
**** Almost seizure free.*
***** 50-75% of seizure frequency reduction.*

The neuropsychological assessment of intelligence at the end of hospital stay (approximately two weeks after surgery) demonstrated an initial decrement from baseline. This temporary decrement did not depend on the dominance or non-dominance of cerebral hemisphere and the number and extent of lesions. Full scale IQ scores were almost equally decreased by 5-7 points two weeks after surgery for the both groups of patients. After this postsurgical period, IQ scores for Group A patients very quickly returned to baseline. For the patients of Group B, this period of rehabilitation was delayed up to four-six months and developed even slower for patients with lower presurgical IQ scores. No remarkable further postsurgical improvement was observed for Group A patients at one and more years after surgery, whereas the increase in full scale IQ for 6-9 points was revealed for the Group B patients after six-eight months of surgery. This improvement was more evident in the patients with preoperative scores higher than 85. Unilateral hippocampal lesions were performed in 55 patients. Seventeen of these 55 were associated with ipsi- and 38/55 with bilateral

amygdalatomies. One-sided hippocampotomy associated with the partial anterior hippocampotomy combined with bilateral amygdalatomy was performed in 21 cases. Subtle changes of formal neuropsychological tests of naming were found for patients with amygdala-hippocampotomy in the dominant hemisphere and were not observed in patients with the left partial anterior hippocampotomy. These changes were more evident in patients with remarkable preoperative language impairment. We did not observe a postoperative decrease of verbal scores after the right amygdala-hippocampotomy and left anterior hippoca-mpotomy, as well as, no decrease of performance scores after the left amygdala-hippocampotomy and right anterior hippocampotomy. Moreover, there was an increase of the appropriate scores, which probably may be attributed to the hemisphere received a surgery limited by volume (anterior hippocampotomy), but eliminating abnormal seizure activity.

Almost total hippocampotomy in one hemisphere and anterior hippocampotomy in another did not lead to profound memory impairment or additional memory problems in our study. Behaviorally evident short-term memory deficit after such bitemporal interventions was observed in four patients for a few days after surgery, leaving the long-term memory unaffected. Patients could not recollect some events, actions, and conversation immediately proceeding the time of testing. These events lasted for 5-7 days after surgery and disappeared abruptly. Mild recent memory deficit compared to the presurgical state were detectable with memory testing for 2-6 months after surgery for 7/21 patients and did not influenced the patient's quality of life. These postsurgical memory declines were quickly reversible in the youngest patients (3/17 6-11 y.o. patients in 6-16 years range). We did not find the substantial difference in short- or long-term memory changes in patients with unilateral amygdala-hippocampotomies and bilateral amygdalatomies combined with unilateral hippocampal lesions.

The most remarkable normalization of the psycho-emotional state and behavioral abnormalities was observed in seizure-free (Engel's Class I, A) and early postoperative seizure (Engel's Class I, B) patients. This improvement was observed almost immediately after surgery during the postoperative hospital stay and remained stable during the follow-up period. Psychotropic medication for these patients was quickly lowered and withdrawn. In patients, who demonstrated seizures reduction by more than for 75% and continue to have considerably less severe seizures the improvement

in the psycho emotional state was evident, but not as remarkable as in seizure-free patients. Behavioral abnormalities in this group of patients became much milder, and these patients demonstrated better psychosocial adjustment. The psychotropic regimen for these patients was significantly lowered, along with their clinical improvement. Patients who improved with respect to seizures by less than a 75% reduction in seizure frequency and failed to have modified seizure activity showed no clinically evident improvements in behavioral or emotional adjustment.

The complete or almost complete psycho-emotional normalization was obtained in patients with interictal chronic depression and anxiety who received amygdalatomies in combination with cingulotomy. The best results were observed with bilateral lesions and in patients, whose presurgical expectations met the outcome in respect of seizures. The effect of surgery was clearly detectable in 2-3 weeks after surgery, and stabilization was usually observed in 6-8 months. The ictal fear, anger attacks, interictal and "preictal" mood changes, irritability, explosiveness and anxiety were better corrected with bilateral amygdalatomies in combination with postero-medial hypothalamotomy and dorso-medial thalamotomy. The remarkable normalization and stabilization of their psycho-emotional state was usually observed immediately after surgery with stabilization in 3-5 months after surgery with some individual differences, depending on the severity of preoperative symptoms, age of patients and surgery success. The histories obtained from the patients' families and the authors' observations during postoperative neurological examinations and EEG evaluations demonstrated that none of the patients showed discernible additional postsurgical deterioration of speech, memory, cognition or behavior.

The scalp EEG dynamics generally followed the course of improvement for seizures. The normalization of postsurgical EEG after the stabilization of the clinical state of the patients of GroupA, was observed in 2/4 Class I and in 2/6 Class II cases. Compared to the preoperative EEGs, no remarkable positive EEG dynamics were observed for the remaining Class I and II patients and for all patients of Classes III and IV. For the patients of Group B, the positive dynamics of postsurgical EEGs were more impressive. The EEG normalization of background activity, disappearance of focal abnormalities, interhemispheric EEG asymmetries, and discontinuation of disseminated sharp activity were observed for 35/44 Class I, 7/11 Class II, and 2/11 Class III (A) patients. Remarkable improvement first in different degrees of normalization of background activity and reducing of sharp focal and diffuse abnormalities were observed for 6/11 Class III and IV patients with no changes in the remaining five. No postoperative EEG worsening was observed during repetitive EEG evaluations. The EEG improvement followed the clinical improvement closely in the patients with preoperative sharp activity overlapping the normal background. The process of EEG normalization in patients with initially abnormal background heralding a focal or diffuse encephalopathy developed slowly with advanced clinical improvement. For 7/10 patients with the presurgical EEG phenomenon of "forced normalization," the postsurgical evaluations revealed the disappearance of this phenomenon along with clinical and EEG improvement.

None of our patients had a worsening of their seizures, psycho-emotional state or behavioral abnormalities after surgery. Previously intractable patients with outcome Classes III and IV became more amenable to medication. No persistent life-threatening complications were observed. Surgical complications included one acute subdural hematoma (10 -15 ml) evacuated during the same surgical session through the burr-hole, one minor thalamic hemorrhage with mild left-sided hemiparesis, which completely resolved in two weeks of intensive care, and three cases of subcutaneous infection successfully treated with antibiotics.

V. Discussion

a) Epileptic focus and epileptic system

A large multicenter study [33] concluded that 77% of intractable epilepsy patients demonstrated 77% of success after mesial temporal lobe resections with a minimal effect on anxiety and depression. Seizures relapsed in 24% of temporal lobe resective epilepsy surgeries. Hennessy et al. [34] found that 35% of seizure relapses came from the contralateral hemisphere and 30% from the contralateral temporal region. These data demonstrate how frequently active elements of epileptic systems remain undetected, and hence persist even with contemporary technically advanced presurgical evaluation. In addition, we have to keep in mind the 30% of intractable epilepsy patients who were not considered for surgery because of multifocality of seizures, localization of epileptic focus (foci) within eloquent cortical areas, or possible postsurgical memory impairment.

The present indications for epilepsy surgery are based on the conception of a single epileptic focus generating the seizure, followed by seizure propagation and involvement of other brain structures. It is suggested that surgical removal of that epileptic focus should make patient seizure free. However, clinical experience and practice demonstrated multifocality of seizures in patients with intractable epilepsy and frequent relapse of seizures after such limited surgeries. This forced the surgeons to expand their surgical tactics, and perform combined resections, or multiple

stereotactic lesions. Multiple lesions seemed to be necessary for the better control of epilepsy [3, 35-39]. Analysis of the literature demonstrates that even conventional resective multilobar and bihemispheric epilepsy surgery [40], combinations of topectomies with multiple subpial transections on both hemispheres, callosotomies and stereotactic amygdala-hippocampotomies [41-44], and multiple cortical thermolesions [45] can be performed without neurological and neuro-psychological complications. Zemskaia et al. [46] performed bilateral one-stage stereotactic interventions on mesiobasal temporal structures or stereotactic operation on one temporal lobe and an open operation on the contralateral temporal lobe in patients with bitemporal epilepsy. These data suggest that the existing conception of an epileptic focus, especially in cases of severe intractable epilepsy, needs additional elaboration.

The concept of an epileptic focus was revised. The difficulty of identifying the precise location of brain structures initiating epileptic seizures has led some authors away from the concept of a strictly localized epileptic focus. A concept of "regional epilepsy" was conceived, which in the case of temporal lobe epilepsy, included orbital, temporal and anterior cingulate areas [47]. The author suggested that the concept of focal epilepsy being related to focal (partial) seizures through one epileptic focus or cortical area is an "overschematized simplicity" and tended to de-emphasize the true complexity of disease and our fragmentary knowledge of the pathophysiology of epilepsy. Collins & Caston [48] concluded that the symptoms of focal epilepsy are not the expression of a single focus, but rather the expression of its associated "circuits." According to Engel [4, 49], in cases of intractable epilepsy the brain of the epileptic patient "appears to be abnormal in many different areas and in many different ways." So et al. [7] found that epileptic seizures arising from the same temporal lobe in the same patient could start independently in larger or smaller areas within a wide epileptogenic zone. Although many authors have articulated the coexistence of discrete epileptic foci in different brain areas, they have not presented the idea of a dynamically organized functional entity or system.

Epilepsy, especially intractable epilepsy, may be considered as a dynamic multifactoral process including alteration in neurotransmitter receptors and synaptical plasticity, ion channelopathies, and reactive autoimmunity [4, 5, 8-13]. This leads to the reorganization of neuronal circuitry and formation of a complex and individually organized epileptic system, including dominant and subdominant epileptic foci and seizure propagating pathways. Chronic and/or intraoperative depth electrode studies have demonstrated the complexity and multistructural organization of epileptic networks in intractable epilepsy patients [7, 13, 30, 50-58]. Wiser [2, 53] and Spencer [13] systematized the results of their studies, subclassified complex partial seizures into several subtypes, and described more or less typical variants of a "cast" of structures participating in the spread and generalization of seizures originating in the temporal lobe mesiobasal structures. It was hypothesized that the epileptogenic circuit for the initiation of seizures is distributed throughout the limbic system with a possible central synchronizing process [8]. Based on this concept, the limbic epilepsy surgery failures were attributed to incomplete resections in seizure circles and more extensive resection of limbic structures with defined contributions from the contralateral limbic system were suggested [59]. Most of the authors described the interrelations of brain structures and seizure propagation variants in general, not in relation to the particular patient to whom these variants were responsible for individual diversity of illness and without a recommendation of individual surgical tactics.

All these data allow us to view severe long-standing intractable temporal lobe epilepsy not as just focal epilepsy, but as focal epilepsy with a dynamically and individually organized epileptic system [3, 11]. The concept of a single epileptic focus generating seizure followed by seizure propagation and involvement the other brain structures should be conceptualized as dominant and subdominant or dormant epileptic foci, and a network including not only pathways and structures involved in the spreading seizure, but actively participating in the epileptic process. Such insight on the problem of surgical treatment of severe long-standing intractable temporal lobe epilepsy dictates a comprehensive evaluation of patients in order to determine the interrelations between the epileptic system core elements and performing an optimal neurophysiologically guided surgical procedure for each patient.

b) Interictal and ictal activity of the epileptic system

The main limiting factor of our study is an inability to have electrodes implanted in all brain structures. We tried to, in some degree, to avoid this factor by a meticulous pre-implantation analysis of the patients' neurological status, seizure manifestations, peculiarities of these manifestations and seizure generalization, and neuro-psychological and imaging data. The analysis of deep temporal lobe electrical activity in both of our groups of long-standing intractable epilepsy patients revealed bilateral involvement of temporal lobe mesiobasal structures in the epileptic process practically in all patients. These data are consistent with results of an SEEG study of another group of our patients [28] where bilateral involvement of temporal lobe mesiobasal structures was found in 66%

of patients. This raises the question of whether such bilateral amygdala-hippocampal involvement is typical for long-standing intractable epilepsy patients, and if it serves, along with other factors (multidrug resistance-associated protein, proteins associated with drug resistance in cancer, major vault protein), as a neurophysiologic basis of epilepsy intractability.

The existence of bilateral independent or propagated epileptic activity was reported at the beginning of the depth electrode era [60-62]. The role of the commissural system and pathways of seizure interhemispheric spread were discussed by many authors [6, 20, 54, 63-66]. Clinical investigations in patients with multicontact electrodes revealed strong evidences that seizure discharges originating in the deep structures of one temporal lobe can spread to contralateral structures without prior involvement of thalamic nuclei or ipsi- and contralateral neocortex [6, 36, 53]. The important role of orbito-frontal cortex in the interhemispheric propagation of temporal lobe seizures was also demonstrated [55, 67]. All of these data indicate that the interaction of brain structures composing an epileptic system may be realized through multiple pathways.

The participation of thalamic nuclei in human epilepsy has been discussed for long time [68-70], more recently with attempts to treat epilepsy with direct brain stimulation [71-77]. In our cohort of patients we, as well as Wieser [54], did not observe an initiation of seizures in thalamic structures, but often recorded thalamic nuclei participation in the propagation of seizures (Figure 4, A) or in the "synchronization" and maintenance of seizure activity in a thalamo-cortical reverberating circle, even after initiating mesiobasal focal activity has ceased (Figure 4, B). This participation of thalamic midline nuclei in the propagation of epileptic seizures is supported by the latest experimental data [78]. A cortico-thalamic coupling of metabolism revealed using the fMRI data, probably detected such variants of thalamic participation in the epileptic process [79].

c) Varieties of surgery and indications for specific types of surgery

All of our surgeries were guided by meticulous analysis of neurophysiologic data obtained during the pre- and intraoperative evaluation of patients. The surgical interventions on the amygdala-hippocampal complexes were considered as "core" surgery, and the lesioning of other brain structures was dictated by the specific clinical, neuropsychological, and electrophysiological peculiarities of each of case. As mentioned above, an apparent unilateral epileptic focus was found in 17% (16/93) of cases. For the remaining 77 patients, bilateral interictal and ictal epileptic activity was assessed as predominantly unilateral in 18 cases (19% of all 93 patients). Unilateral surgeries were performed in all 31 patients of Group A (surgery types 1-6) and 17 patients of Group B (surgery types 9-11). During amygdala-hippocampotomies, we usually tried to perform a total or subtotal lesion of these structures, keeping in mind that small amygdalar lesions might be insufficient to control seizures [80]. This opinion was later supported by comparison of outcomes of stereotactic amygdala-hippocampotomy in one group of patients with lesions encompassing amygdala and 13-21mm (mean 16.8 mm) of anterior hippocampus, with another group of patients to whom anterior hippocampal lesion was extended to15-34 mm (mean 21.5 mm) [81]. The difference just of 4.7 mm gave a threefold increase in favorable results. The therapeutic effect of amygdalatomy is not only the lesion of an epileptogenic tissue and normalization of psycho-emotional state and behavior, but also prevents the spread of seizure discharges from the amygdala-hippocampal complex to the frontal lobe through the fasciculus uncinatus [82]. This may explain, in part, the success of amygdalatomy against epileptic seizures in some cases when the hippocampus was left intact [83, 84]. The second important peculiarity is that homolateral amygdala and hippocampus are practically always involved together in epileptogenesis. The hippocampus was considered as a core part of the "medial emotional circle" [85]. Later, the "baso-lateral emotional circle" was described with the amygdala as its important part [86]. In epilepsy, besides seizure generation, the combined abnormal functioning of these two structures is responsible for psycho-emotional and behavioral abnormalities, and makes both of these structures important double targets for the treatment of intractable epilepsy patients with psycho-emotional and behavioral disturbances.

In the patients with interictal, preictal, and postictal psycho-emotional disturbances, the thalamic, hypoth-alamic, and limbic cortical structures are consistently involved in the epileptic process. Recent studies found that postictal psychoses in partial epilepsy is associated with broadly and bitemporally distributed epileptogenic network [87]. Our previous investigations with chronically implanted electrodes demonstrated a direct interrelation between amygdalar and hippocampal activity and exacerbation of psycho-emotional abnormalities in epileptic patients [3, 88]. It was concluded that ictal fear is related to pathology of the amygdala and that it, like the hippocampus, is an important substrate of temporal lobe epilepsy [89]. Later, metabolic changes were described in the head of the hippocampus in patients with ictal fear [90]. Cingulate participation in partial epilepsy was reported earlier [91, 92]. We found that cingulate involvement in the process of seizure generalization was frequently observed in patients with psycho-emotional disturbances, especially with depression and anxiety as

a major complaint confirmed with neuro-psychological testing. This cingulate involvement was usually characterized by rapid contralateral cingular spread and subsequent spread to the frontal cortex. Thalamic dorso-medial nucleus (DM) and postero-medial hypothalamus are frequently involved in the seizure spread in patients with interictal, preictal fear and rage attacks, postictal twilight states and hypersexual behavior.

The difference between Group B patients who underwent unilateral surgery is that in addition to amygdala-hippocampotomy, cryo-lesions in CM and fornix (type 9 surgery), CM and Forel-H-field (type of surgery 10), and DM, PMH, and fasciculus uncinatus (type of surgery 11) were performed. CM lesions were performed because of SEEG verified participation of this nucleus in the propagation and synchronization of seizure activity (Figure 4). Fornicotomy was performed because of frequent secondary generalization of seizures and SEEG-verification of fornical involvement (Figure 2). Forel-H-tomy was performed because of fast secondary seizure generalization after spread over ipsilateral frontal cortex and fornix preceding contralateral involvement. DM and postero-medial hypothalamic lesions were performed on patients with major psycho-emotional disturbances and SEEG verification of the involvement of these structures in the epileptic process. Fasciculus uncinatus lesions were performed because of fast clinical generalization of unilateral focal seizures and predominant involvement of homolateral fronto-temporal areas in the seizure spread (Figure 5).

The same criteria of choosing additional targets inside the epileptic system were used during bilateral surgeries with some additional peculiarities. Bilateral amygdalotomy was performed for all 59 bilateral surgery patients of Group B (surgery types 1-8). The indications for bilateral amygdalatomy were a high level of interictal epileptic activity in both amygdalae without obvious prevalence, participation in subclinical and clinical seizures developing in both temporal lobes, and, in most cases, evident psycho-emotional disturbances. For the 21 patients of Group B, we performed total hippocampotomy on one side and partial anterior hippocampotomy on the contralateral side (surgery types 6-8). The criteria to perform these asymmetric surgeries on both hippocampi were apparent bitemporal independent EEG/SEEG onset of seizures in both hippocampi, the distinctive manifestations of the clinical seizures, and mutually suppressive interactions of hippocampal epileptic foci, heralding possible activation of another hippocampal epileptic focus after the ablation of one of them [28, 31]. Before performing full-size partial anterior hippocampotomy, we undertook an additional study of 10 similar patients (not included in this series) with small control electrolytic anterior hippocampal lesions ranging in diameter from 2 to 8 mm. Postsurgical neuro-psychological testing did not reveal additional memory deficits, compared with their preoperative state.

f) Surgery outcomes regarding the seizures and psycho-emotional abnormalities

A relapse of seizures in patients with Class I-III outcomes was observed in 7 patients (12%). The relapse of seizures during 1-5 years of follow-up is higher than that recently reported (4%) after temporal lobe resective surgery [93], but there is a considerable difference between the groups of patients and indications for surgery. These results, comparable to resective temporal lobe epilepsy surgery results, are obtained with patients who usually remain beyond the scope of indications for surgery and do not expect any help.

The comparison of outcomes with respect to seizures in Group A and Group B (Table 3) demonstrates considerably better results for group B, especially for Engel's Classes I and II (free of seizures and rare seizures). These data indicate that the efficacy of multitarget lesioning of the key elements of the epileptic system is comparable (Table 6) with the 46% to 78% of successful results of temporal lobectomy in patients with strongly localized unilateral temporal lobe epileptic foci [14, 33, 94, 95].

The main obstacle and concern with epilepsy surgery of patients with poorly localized or bitemporal epileptic foci, suggesting a multifocality of seizures, psycho-emotional and psycho-social problems, are a dread of such surgery complications as memory and personality impairment. This fear stems from Klüver & Bucy's [96] findings, which demonstrated that bilateral resection of temporal lobes including temporal lobe cortex, hippocampus, and amygdala produces a "psychic blindness" syndrome in monkeys. Later, Scoville [97], and Scoville & Milner [98] described recent memory loss after bilateral hippocampal lesions. A review of these cases did not reveal a precise surgery limited with hippocampal ablations, but rather extensive bilateral resection of the medial surface which extended 8 cm posteriorly from the tip of temporal lobe, performed through Scoville's bilateral fronto-orbital approach. Terzian & Ore [99] described bilateral temporal lobe resections both extended up to the vein of Labbe in a patient with bilateral independent EEG epileptic foci who exhibited some elements of Klüver-Bucy syndrome associated with severe memory loss. Apparently, the volumes of these surgeries, number and extend of bilaterally resected temporal lobe structures including lateral, basal cortex, hippocampal, parahippocampal gyri and entorinal cortex are not comparable with precise and controllable stereotactic lesions, which do not include the whole extent of both hippocampi. The dependence of the degree of

cognitive, learning, and memory functions on the degree of surgical intervention and surgical approach was also reported by Wieser & Yasargil [100], who found less or even no impairment after selective amygdala-hippocampectomy compared to anterior temporal lobectomy. Many authors attribute the memory impairment after experimental or clinical temporal lobes ablation to the different parts of temporal lobe cortex. Ojemann & Dodrill [101] emphasized the importance of temporal lobe lateral cortex for verbal memory. Joo et al. [102] found that the resection of inferior and basal temporal lobe gyri leads to an impairment of verbal memory. Halgren et al. [103] recorded neuronal unit activity in the mesiobasal structures during psychological tests and found that only hippocampal gyrus neurons responded during recent memory recall.

The participation of specifically hippocampal gyrus in recent memory mechanisms is confirmed by intact recent memory after bilateral fornicotomy [104, 105] and with disrupting memory with cingulum stimulation [106].

The almost total hippocampotomy in one hemisphere and anterior hippocampotomy in another without any additional lesions in temporal lobe cortex, especially the hippocampal gyrus, did not lead to profound memory impairment or additional memory problems in our study. Behaviorally evident short-term memory deficit after such bitemporal interventions was observed in four patients a few days after surgery, leaving long-term memory unaffected. We did not find a substantial difference in short- or long-term memory changes in patients with unilateral amygdala-hippocampotomies and bilateral amygdalatomies combined with unilateral hippocampal lesions. The elucidation of mild or moderate postsurgical memory changes in the most of our patients was probably impeded because of their presurgically impaired memory. Such subtle postsurgical memory changes might be explained with continuous or intermitted discharges in the amygdala- hippocampal complex already functionally "resected" these structures, and their real surgical ablation did not add a further deficit. We did not observe a postoperative decrease of verbal scores after right amygdala-hippocampotomy and left anterior hippocampotomy, as well as no decrease of performance scores after left amygdala-hippocampotomy and right anterior hippocampotomy. Moreover, there was an increase of these scores of a few points, probably because of an absence or decrease of a disturbing influence of intermitted or constant epileptic activity in the contralateral epileptic focus. The amelioration and return to normal social life and in some cases even rise in IQ for epileptic patients after bilateral amygdalatomy and unilateral hippocampotomy have been reported [107, 108].

Persistant abnormal activity in mesiobasal temporal lobe structures has the same disturbing effect on cognitive, learning, and memory function as their ablation. Transient retrograde amnesia was also observed after widespread disruption of the mesial temporal lobe by electric stimulation [109, 110] . It is found that subclinical discharges may be associated with transitory cognitive impairment detectable by appropriate psychological testing [111] In epilepsy patients with implanted depth electrodes, it was found that fast spiking in the hippocampus might be responsible for the memory deficits in patients with epilepsy [112]. These data support the hypothesis that subclinical epileptic activity in the hippocampus disables its normal functioning and may simulate its "functional ablation." The absence of substantial difference in short- or long-term memory changes in patients with unilateral amygdala-hippocampotomies and bilateral amygdalatomies combined with unilateral hippocampal lesions suggests limited amygdala participation in the processes of memory. We already reported successful stereotactic amygdalatomy in 8/14 bitemporal epilepsy patients who developed an activation of the contralateral epileptic foci after temporal lobotomy [28]. These results are supported by data that even large bilateral amygdala lesions fail to affect learning or retention of verbal materials [113].

Seizure-free patients achieved significant and stable improvements in behavioral and emotional adjustment approximately six months after surgery, whereas in patients with less favorable outcomes for seizures this adjustment was less evident and stabilized at lower level in eight months to one year. In 10 patients with presurgical anger attacks, aggression, periodic psychotic states, and EEG phenomenon of "forced normalization" [114], postsurgical evaluations revealed the disappearance of this phenomenon for seven patients, along with clinical and EEG improvement. SEEG evaluations revealed a high level of interictal and ictal epileptic activity in the amygdala with involvement of the posterior hypothalamus thalamic dorso-medial nucleus. Our previous studies performed with chronically implanted deep electrodes demonstrated that despite the "normalization" of the scalp EEG, anger attacks, destructive behavior, and sexual aggression are consistent with increased intermittent epileptic activity and "subclinical" epileptic seizures in temporo-limbic structures [115]. These findings are important in terms of clinical, EEG, and behavioral assessment of the results of surgery. For patients who exhibited a reduction or complete cessation of convulsive or psychomotor seizures after surgery with evident EEG improvement, but demonstrate unchanged or increased psycho-emotional and behavioral disturbances, it is necessary to be careful with the final assessment of surgery outcome. This group of patients represents a "group of risks," and relapse of clinical seizures in this group may be more likely.

VI. Conclusion

Our results demonstrate that multitarget electrophysiologically guided stereotactic surgery can have a beneficiary effect on seizure frequency and severity, normalize psycho-emotional state and behavior in long-standing intractable epilepsy patients who, in most cases are not considered as optimal candidates for resective epilepsy surgery. Correctly and carefully planed multitarget stereotactic surgery does not necessarily lead to additional and stable postoperative declinies in intelligence, learning, and especially memory, and the benefits of seizure control definitely outweigh the risk of further cognitive decline. Moreover, according to the extent of surgery and results obtained, this tactic can be considered as a minimally invasive approach to intractable epilepsy surgery. This article does not intent to replace resective epilepsy surgery when it can be highly beneficial. The aim of this study is to advocate the resurgence of electrophysiologically guided stereotactic lesional epilepsy surgery, based on practically applied existing knowledge about sophisticated epileptic systems in cases of severe intractable epilepsy, as well as, the implementation of more effective lesional methods. This approach to epilepsy surgery may include different reasonable combinations of resective, stereotactic lesional, stimulation and cortical transection techniques directed toward beneficiary treatment of these intractable epilepsy patients.

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We confirm that we have read the Journal's position on issues involved in ethical publications and affirm that this report is consistent with these guidelines.

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Bourneville Tuberous Sclerosis- Difficulties of the Diagnosis- A Case Report

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Abstract- The diagnosis of Bourneville Tuberous Sclerosisthe„ forme fruste"- was established for a sixteen years old teen-ager, due to some typical cutaneous lesions, of angiofibromas type, wich appeared at puberty, lesions suggestive for the diagnosis.

The imagery investigations confirmed the existence of the brain hamartomas and of the angiomyolipomas of the kidneys, supporting the diagnosis of Bourneville disease.

Keywords: *bourneville tuberous sclerosis.*

GJMR-A Classification : *NLMC Code: WL 348, WM 140*

Strictly as per the compliance and regulations of:

Bourneville Tuberous Sclerosis- Difficulties of the Diagnosis- A Case Report

Mihaela Lungu [α] & Alina Ursoiu [σ]

Abstract- The diagnosis of Bourneville Tuberous Sclerosis- the „ forme fruste"- was established for a sixteen years old teen-ager, due to some typical cutaneous lesions, of angiofibromas type, wich appeared at puberty, lesions suggestive for the diagnosis.

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I. Case Report

The patient C.A., sixteen years old, female, takes notice of the appearance-approximately two years ago- of some cutaneous lesions on the chin, initially considered by herself to be acne vulgaris. These lesions were the only signs which determined her to ask for a medical examination, the teen-ager having no other complaints.

In her personal history there are no diseases and in her family history we find 4 healthy brothers and no hereditary pathology. Anamnesis excludes epilepsy and mental retardation.

The cutaneous lesions have a typical aspect of angiofibromas, with a red colour, are situated in the chin region- those with a bigger size, maximum 2 mm, in the nasogenian folds and on the cheeks, where the lesions have small dimensions. These lesions are firm on palpation and they are not accompanied by other symptoms (pain, prurigo). The clinical aspect is of angiofibromas (fig.1).

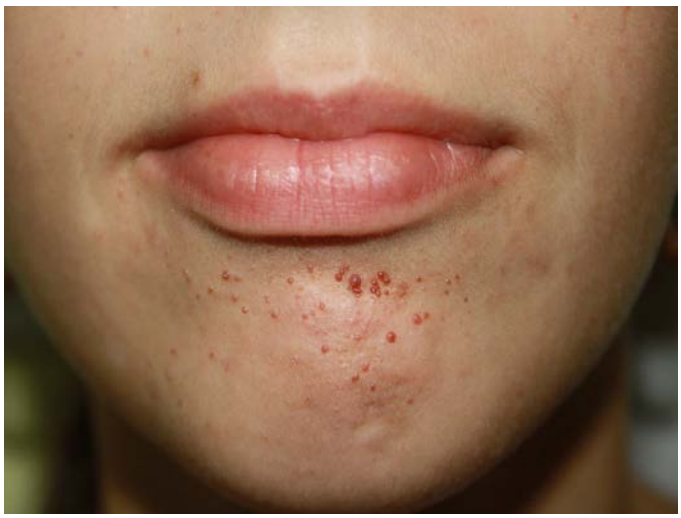

Fig.1 : Angiofibromas

The general clinic examination, the neurological examination and the examination of the fundus of the eye were normal.

The cutaneous lesions raise the suspicion of Bourneville Tuberous Sclerosis, for this reason indicating imagistic investigations.

On the CT examination of the brain there are found hyperdense formations with the diameter of 2, 4 and 5 mm, subependymally situated in the sidewall of the third ventricle, with a typical aspect of hamartomas (fig.2)

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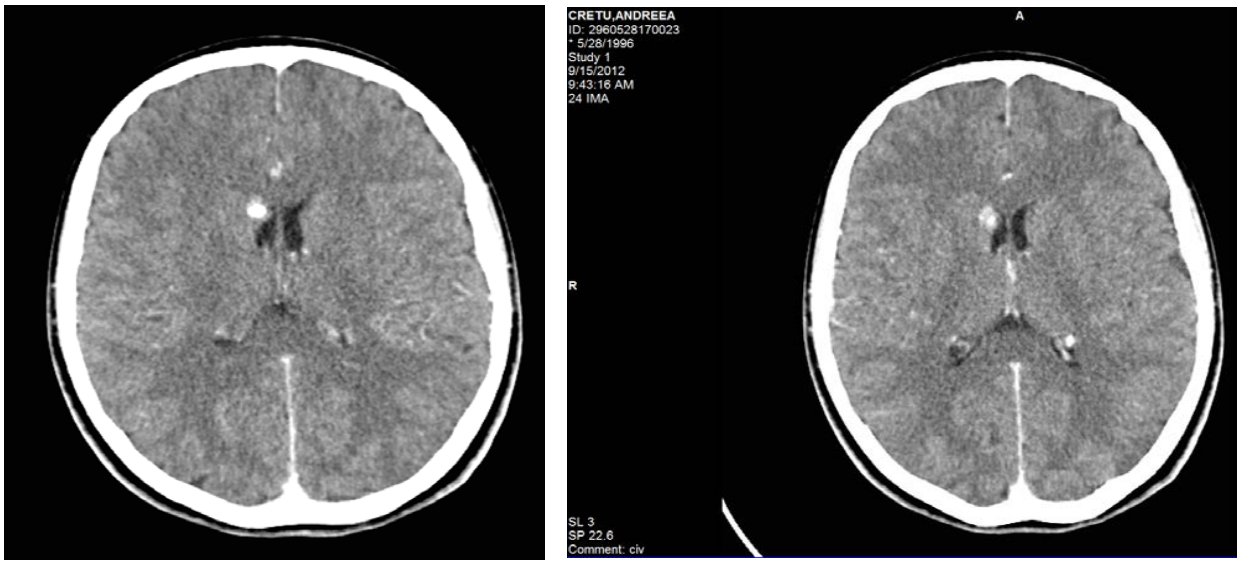

Fig. 2 : Subependymally hamartomas

The abdominal-pelvic CT examination shows multiple formations with a fatty density included, with diameters between 2-6 mm, situated on the cortical zone of the kidneys, on both sides. In the left kidney it can be visualized a pericalyceal superior formation of 18 mm diameter, which highly captures the contrast substance, compatible with an angiomatos lesion (fig.3) The thoracic CT and the echographic examinations of the heart exclude lungs or heart lesions.

The conclusions of the imagistic investigations are: brain hamartomas and angiomyolipomas of both kidneys.

These lesions, typically associated with the cutaneous angiofibromas, allow the diagnosis of Bourneville Tuberous Sclerosis.

The differential diagnosis was made with other forms of facomatosis (neurofibromatosis) and with other dermatological diseases (acne vulgaris, trichoepiteliomas, syringomas).

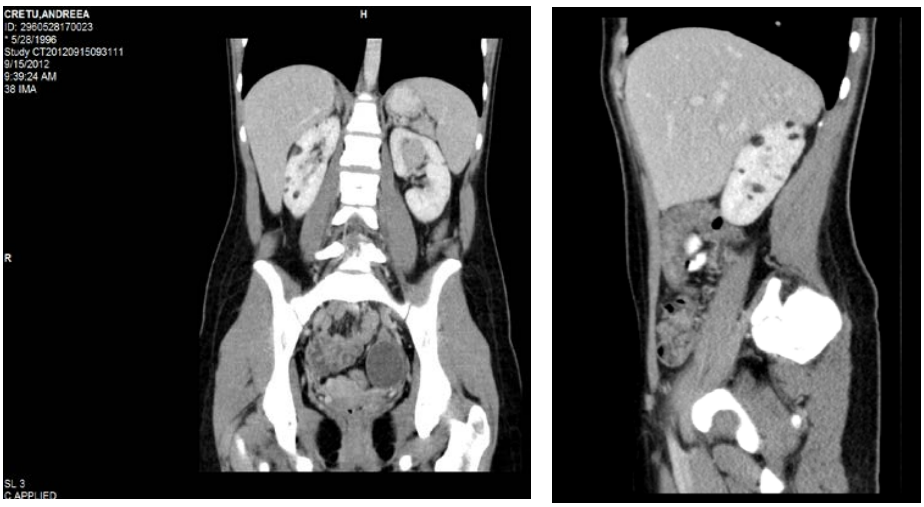

Fig. 3 : Angiomyolipomas of the kidneys

II. Discussions

The typical cutaneous lesions (angiofibromas) raised the suspicion of Borneville disease, later confirmed by the imagistic investigations.

A „forme fruste" of Bourneville Tuberous Sclerosis was confirmed, in a sporadic case, without epilepsy or mental retardation, with typical cutaneous lesions and multiple tumors of the brain and the kidneys.

The case is a sporadic one, the patient having 4 healthy brothers (needed to be investigated). In the Bourneville disease, the heredity is proved in 14-50 percent of the cases.

The forme fruste of Bourneville disease is mentioned in the neurological literature to be frequent.

The therapy focuses on the neurological observation (risk of refractory epilepsy), genetic advise, professional orientation.

The treatment of the angiofibromas is limited to more or less invasive methods: cryotherapy, surgery, laser phototherapy, methods which are frequently followed by the reappearance of the lesions and complications (keloid scars). A very recently case study proposes for therapy the application of an immunosuppressive agent, of a new generation, with good results, but there are necessary randomised studies to confirm the safety of a long time treatment.

Bourneville Tuberous Sclerosis is an inherited disease of an autosomal dominant type, with a high level of new mutations, characterized by multifocal tumors, malformations and typical cutaneous lesions. The locus for the genetic mutations are 9q34 and 16p34.

It is clinically characterized by the triad: refractory epilepsy, mental retardation (sometimes severe) and angiofibromas of the face (typical for 70-90 percent of the patients, along with other types of cutaneous lesions). In the brain, there are hamartomas and calcified tubers nodules (cortical brain stones), which determine refractory epilepsy and hydrocephalus. The neurons have three to four normal size. There are also lesions which involve other types of cells: fibroblasts, cardiac myoblasts, angioblasts, developed in an excessive number and size. These are the causes of the appearance of angioleiomyomas of the kidneys, liver, tests, adrenal gland, rhabdomyomas of the heart, retinal glial nodules. It is presupposed that some inhibitory growth factors are blocked at a certain stage of the embryonic life, fact which leads to the hyperplasia and hypertrophy of the well-differentiated cells.

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Homocystinemia Leading to Bright Facial Colliculus - A Rare Entity in Young Adults

By Suresh Kumar, Sudhir Sharma, Sanjiv Sharma & R G Sood
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Introduction- The facial colliculus is an elevated area located on the dorsal pons in the floor of the 4th ventricle. It is produced by the nucleus of the abducens nerve and the flexure of the facial nerve around it. Any lesion involving the abducens nucleus cause the disorder of internuclear ophthalmoplegia (INO) which is characterized by ipsilateral adduction deficit and the preservation of abduction of the contralateral eye when the patient tries to look in the contralateral direction. Isolated infarction of facial colliculus effecting abducens nucleus is very rare [1].

GJMR-A Classification : NLMC Code: WS 340

Homocystinemia Leading to Bright Facial Colliculus - A Rare Entity in Young Adults

Suresh Kumar [α], Sudhir Sharma [σ], Sanjiv Sharma [ρ] & R G Sood [ω]

I. Introduction

The facial colliculus is an elevated area located on the dorsal pons in the floor of the 4th ventricle. It is produced by the nucleus of the abducens nerve and the flexure of the facial nerve around it. Any lesion involving the abducens nucleus cause the disorder of internuclear ophthalmoplegia (INO) which is characterized by ipsilateral adduction deficit and the preservation of abduction of the contralateral eye when the patient tries to look in the contralateral direction. Isolated infarction of facial colliculus effecting abducens nucleus is very rare [1].

II. Case Report

A 27 year-old right handed male presented with history of sudden onset of headache, giddiness and double vision with deviation of left eye outward. Ocular examination showed normal size of bilateral pupils with prompt direct light reflexes. His left eye was abducted (Figure 1), and he was not able to adduct right eye. There was nystagmus of left eye. Rest of the neurological examination was normal. MRI brain done which revealed bright spot on diffusion weighted imaging in right facial colliculus consistent with acute infarct (Figure 2). Retrospectively his blood analysis showed homocystinemia with homocysteine level of 43.15 μ mol/l.

Figure 1 : Shows abduction of left eye at rest

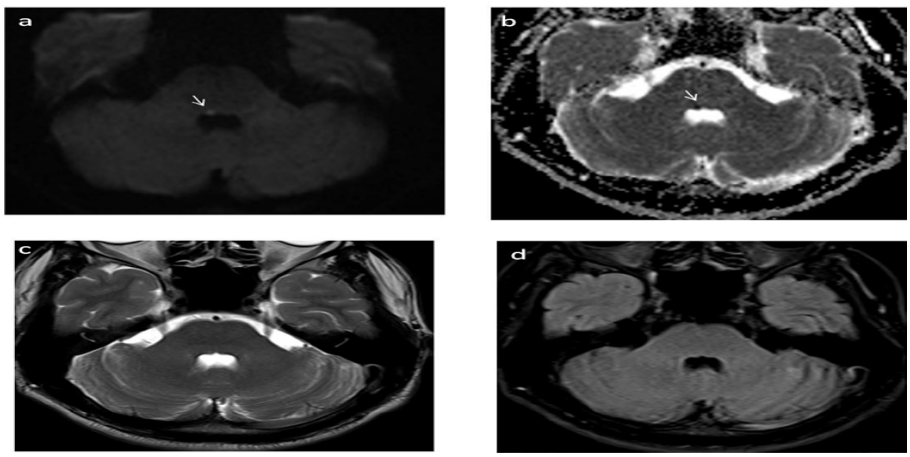

Figure 2 : Reveals bright right facial colliculus on Diffusion weighted imaging (a with white arrow),corresponding apparent diffusion coefficient image showing this area dark .No abnormal signal intensity appreciated on T2W (c) and Fluid attenuated inversion recovery image(d).

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III. Discussion

The facial colliculus involvement leading to INO may occur in various disorders like demyelination, nutritional deficiencies, vascular diseases, tumor, infection, hydrocephalus and trauma[2]. The demyelination and infarction are the most common pathophysiologies among all [3]. The pathogenesis of infarction in the brain stem is due to small-vessel occlusion secondary to athermanous disease of posterior circulation like basilar artery or posterior cerebral arteries. The atherosclerotic disease is usually seen in older patients. The metabolic disorder like elevated plasma homocysteine is a rare entity which is associated with risk of ischemic stroke [4]. FathBender & Evers et al, reported that homocysteine injures small perforating arteries and cause lacunar infarction in patients [5, 6]. Our patient also presented with focal infract of right facial colliculus secondary to elevated plasma level of homocysteine. The importance of presenting this case is that patients presenting with small vertebrobasilar lesions are likely to have negative imaging features. This failure to detect acute lesions may be attributable to factors such as perforating arteries feed very small areas of the brain stem, and magnetic susceptibility artifacts occurring near brain stem cause distortions in spatial resolution and blurred image analysis [7]

Our case is unique in the sense that there was small lacunar infarct involving right facial colliculus in young adult and this was secondary to elevated plasma level of homocysteine which itself a rare cause of stroke. Thus while evaluating young patients of stroke these rare disorders should be kept in mind and brain imaging to be evaluated with great care.

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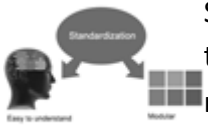

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Before start writing a good quality Computer Science Research Paper, let us first understand what is Computer Science Research Paper? So, Computer Science Research Paper is the paper which is written by professionals or scientists who are associated to Computer Science and Information Technology, or doing research study in these areas. If you are novel to this field then you can consult about this field from your supervisor or guide.

TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

6. Use of computer is recommended: As you are doing research in the field of Computer Science, then this point is quite obvious.

7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

8. Use the Internet for help: An excellent start for your paper can be by using the Google. It is an excellent search engine, where you can have your doubts resolved. You may also read some answers for the frequent question how to write my research paper or find model research paper. From the internet library you can download books. If you have all required books make important reading selecting and analyzing the specified information. Then put together research paper sketch out.

9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

13. Have backups: When you are going to do any important thing like making research paper, you should always have backup copies of it either in your computer or in paper. This will help you to not to lose any of your important.

14. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several and unnecessary diagrams will degrade the quality of your paper by creating "hotchpotch." So always, try to make and include those diagrams, which are made by your own to improve readability and understandability of your paper.

15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.

- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
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What to stay away from

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- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
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- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

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- To guard yourself and others from possible illegal use please do not permit anyone right to use to your paper and files.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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