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Carotid Intracranial Stenosis

Psychoactive Substance Dependence

Highlights

Clinical and Radiological Profile

Retinal Changes in Cerebral Malaria

Discovering Thoughts, Inventing Future

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Contents of the Issue

i. Copyright Notice
ii. Editorial Board Members
iii. Chief Author and Dean
iv. Contents of the Issue

1. Stroke Subtypes and Intracranial Large Vessel Stenosis Clinical and Radiological Profile. *1-6*
2. Neuro form EZ Stent for Late Thrombosis after Carotid Intracranial Stenosis: A Case Report and Literature Review. *7-13*
3. Validation of Psychoactive Substance Dependence. *15-19*
4. Neurological Manifestations among Patients with HIV – Active Tuberculosis Co Infection. *21-26*
5. Maniology. *27-32*
6. Evoked Brain Potentials in the Preoperative Diagnosis of Type 1 Chiari Malformation. *33-48*

v. Fellows
vi. Auxiliary Memberships
vii. Preferred Author Guidelines
viii. Index

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Stroke Subtypes and Intracranial Large Vessel Stenosis Clinical and Radiological Profile

By Mohammad Osama Abdulghani, Hani Moahamed Aref, Azza Abdulnasser, Karima Moustafa Maher, Amr Abd El Monaem & Mohamed Ahmed Shafik

Ain Shams University

Abstract- *Objective:* This study aimed at to identify stroke subtypes, clinical picture, outcome, prevalence of stroke-related risk factors and the prevalence of Intracranial(IC) large vessel Stenosis in ischemic stroke Egyptian patients.

Materials and Methods: 504 consecutive acute cerebral stroke patients were enrolled to a prospective hospital-based study during a period of one year and submitted to clinical evaluation including National institute of health stroke scale (NIHSS), Modified Rankin Scale (MRS),baseline computed tomography (CT) scan, magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA).

Results: The study revealed that 479 patients (95%) of study cases were ischemic strokes, 25 patients (5%) of study cases were primary Intracerebral Hemorrhage (ICH). Subtypes of acute ischemic stroke were: lacunar stroke 54.4 %. Large artery atherosclerosis 32.0 %. Cardio embolic 4.0 %. Undetermined etiology 8.9 %. Other determined etiology 0.7%.

Keywords: *stroke subtypes; stroke risk factors; IC large vessel stenosis.*

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Stroke Subtypes and Intracranial Large Vessel Stenosis Clinical and Radiological Profile

Mohammad Osama Abdulghani [α], Hani Moahamed Aref [σ], Azza Abdulnasser [ρ], Karima Moustafa Maher [ω], Amr Abd El Monaem [¥] & Mohamed Ahmed Shafik [§]

Abstract- Objective: This study aimed at to identify stroke subtypes, clinical picture, outcome, prevalence of stroke-related risk factors and the prevalence of Intracranial(IC) large vessel Stenosis in ischemic stroke Egyptian patients.

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Results: The study revealed that 479 patients (95%) of study cases were ischemic strokes, 25 patients (5%) of study cases were primary Intracerebral Hemorrhage (ICH). Subtypes of acute ischemic stroke were: lacunar stroke 54.4 %. Large artery atherosclerosis 32.0 %. Cardio embolic 4.0 %. Undetermined etiology 8.9 %. Other determined etiology 0.7%. Median NIHSS score on admission was (7), Median NIHSS on discharge was (4). Median MRS score on admission was (3), Median MRS score on three months follow up was (1). The most prevalent risk factor for stroke was Hypertension (HTN) 70.1%, followed by Diabetes mellitus (DM)53%, Heart diseases(HD) 35.4%, with Ischemic Heart diseases (ISHD)22%, Atrial fibrillation (AF) 5.9 %, Myocardial infarction(MI) 1.4%. Past history (PH) of stroke 30.4%. Smoking 25.7%.Hyperlipidemia 8.9%. PH of Transient Ischemic Attacks (TIAs) 8.7%. PH of ICH 2.4%. (35.4%) of cases showed patent IC large vessels by MRA. (27.4%) of cases showed IC large vessel with (<50% stenosis). (22.9%) of cases showed IC large vessel with (>50% stenosis). (14.3%) of cases showed a totally occluded IC large vessel.

Conclusion: Ischemic stroke is the most prevalent type of stroke (95%), Lacunar stroke (54.4%) is the most prevalent ischemic stroke subtype, HTN (70.1%) is the most prevalent risk factor for stroke. IC large vessel stenosis was prevalent among (64.6%) of study cases.

Keywords: stroke subtypes; stroke risk factors; IC large vessel stenosis.

I. Introduction

Stroke is a common neurological disorder, the second commonest overall cause of death, and a major cause of disability in survivors.[1,2] Cerebrovascular disease is globally the sixth commonest cause of an ongoing disease burden, but is expected to move to the fourth place by 2020,Over65% of stroke deaths are reported from developing countries.[3,4]

Stroke is largely preventable, so that knowledge of risk factors is essential to achieve a reduction in the stroke rate and resulting diseaseburden.[5] Examination of stroke incidence, prevalence, subtypes, risk factors and outcome in various countries is therefore an important foundation for evidence-based prevention programs.[5]

Although epidemiologic studies on stroke were carried out in different parts of the world including some neighboring Arab countries, there were no published data from Egypt.[5]

II. Subjects and Methods

A total of 504 patients, admitted to A in Shams University Specialized Hospital stroke unit during the period from January 2011 to March 2012 with a diagnosis of acute cerebral stroke, were subjected to the following:

- Detailed medical history taking.
- Complete neurological examination with NIHSS score and m RS score.
- CT brain without contrast for all study patients within 30 minutes of clinical suspicion of a stroke at the emergency room(ER) to differentiate acute cerebral infraction from anacute cerebral hemorrhage.
- MRI brain Stroke protocol for 456 patients of the study group within 24 hours of patient admission to the hospital. This protocolin cluded T1-weighted image (T1WI), T2-weighted image (T2WI), fluid-attenuated inversion recovery (FLAIR) image, diffusion weighted image (DWI), gradient-echo (T2*) weighted image MRI scans in addition to TOF MRA.
- Noncontrast 3 Dimensional time of flight (TOF) MRA for anterior and posterior circulation with "collapsed image" films were read and evaluated by Neurology-Radiology team for consensus and agreement of our independent observation of the presence of intracranial (IC) large vessel arterial stenosis or occlusion in (2 Internal Carotid Arteries ICAs, 2 Middle Cerebral Arteries MCAs, Basilar artery BA, 2 Posterior Cerebral Arteries PCAs) among 314 patients of the study group.
- TOF MRA Stenotic lesions are sites where flow signal intensity loss commonly occurs. Stenosis was visually

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estimated and calibrated according to the residual lumen diameter measured at the site of maximum narrowing and the diameter of the adjacent normal vessel, from which the percentage stenosis was estimated. Significant stenosis was considered if it was more than 50%.[6,7]

- Based on the above information, ischemic strokes were classified according to Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification into one of 5 categories based on risk factors as well as clinical and brain imaging features: large artery atherosclerosis, cardio embolic strokes, small vessel occlusion (lacunar strokes), undetermined etiology stroke or other determined etiology stroke.[8]
- The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 15.0.1 for windows; SPSS Inc, *Chicago, 2001).*
- Data was presented and descriptive statistical analysis was done according to the type of data obtained for each parameter:
  - Mean, Standard deviation (± SD) and range for parametric numerical data.
  - Frequency and percentage of non-numerical data.

III. Results

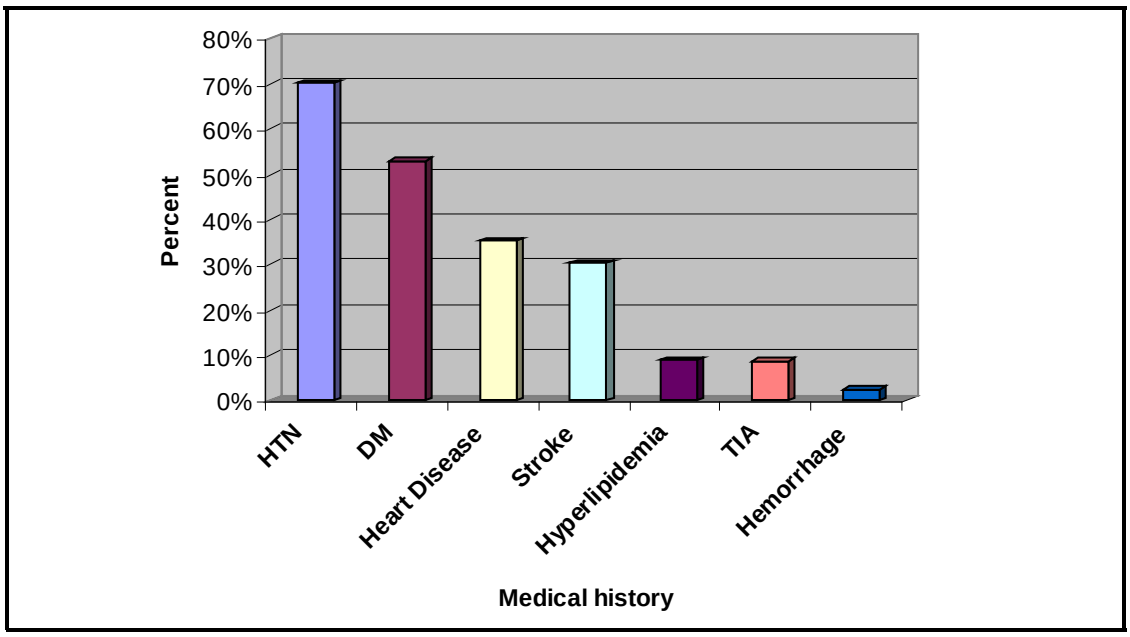
504 stroke patients were enrolled to this hospital-based study with the following results:

Table 1: Description of socio-demographic data and past history of risk factors for stroke among study patients

		N	%
Age (years)	Mean ±SD	63±10.9	
	Range	28-90	
Sex	Male	338	67.1%
	Female	166	32.9%
Alcohol	Yes	2	0.4%
	No	478	99.6%
Smoking	Non smoker	285	59.0%
	Smoker	124	25.7%
	Ex-smoker	74	15.3%
DM	Yes	263	53.0%
	No	233	47.0%
HTN	Yes	349	70.1%
	No	149	29.9%
PH Heart Disease	Yes	174	35.4%
	No	317	64.6%
Type of Heart Disease	No	317	64.6%
	AF	29	5.9%
	ISHD	108	22.0%
	MI	7	1.4%
PH hyperlipidemia	Yes	43	8.9%
	No	441	91.1%
PH stroke	Yes	150	30.4%
	No	344	69.6%
PH TIA	Yes	43	8.7%
	No	451	91.3%
PH Hemorrhage	Yes	12	2.4%
	No	482	97.6%

Table (1) shows that the mean age of study cases was (63±10.9 years). Males represented (67.1%) of study cases. The most prevalent risk factor for stroke among study cases was HTN (70.1%), followed by DM (53%), and Heart diseases (35.4%) with ISHD representing (22%), then AF (5.9%), and MI (1.4%). PH of hyper lipidemi a was present among (8.9%) of study cases. PH of stroke was present among (30.4%) of study cases. Smokers (25.7%). PH of TIAs was found among (8.7%) of study cases. PH of cerebral hemorrhage among (2.4%) of cases. And alcoholics (0.4%) as the least prevalent risk factor (Graph 1).

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Graph 1: Prevalence of PH of Risk Factors for stroke among study cases

Table 2: Description of acute cerebral stroke by C.T brain findings

		N	%
CT brain	Ischemic	479	95.0%
	Hemorrhagic	25	5.0%

Table (2) shows that 479 patients (95%) of the study cases were ischemic strokes by C.T brain findings, while only 25 patients (5%) of study cases were hemorrhagic strokes.

Table 3: Description of stroke cases by clinical NIHSS and MRS scales on admission, discharge and on follow up

	N	Mean	±SD	Minimum	Maximum	Median
NIHSS on admission	476	7.97	4.91	1.00	27.00	7.00
NIHSS on discharge	391	4.87	3.47	.00	18.00	4.00
MRS on admission	465	3.16	1.33	.00	5.00	3.00
MRS on 3 months	340	1.87	1.38	.00	5.00	1.00

Table (3) shows that the mean NIHSS on admission was (7.97±4.91) with median score (7), while the mean NIHSS on discharge was (4.87±3.47) with median score (4). The mean MRS on admission was (3.16±1.33) with median score (3), while the mean MRS on 3 months follow up was (1.87±1.38) with median score (1).

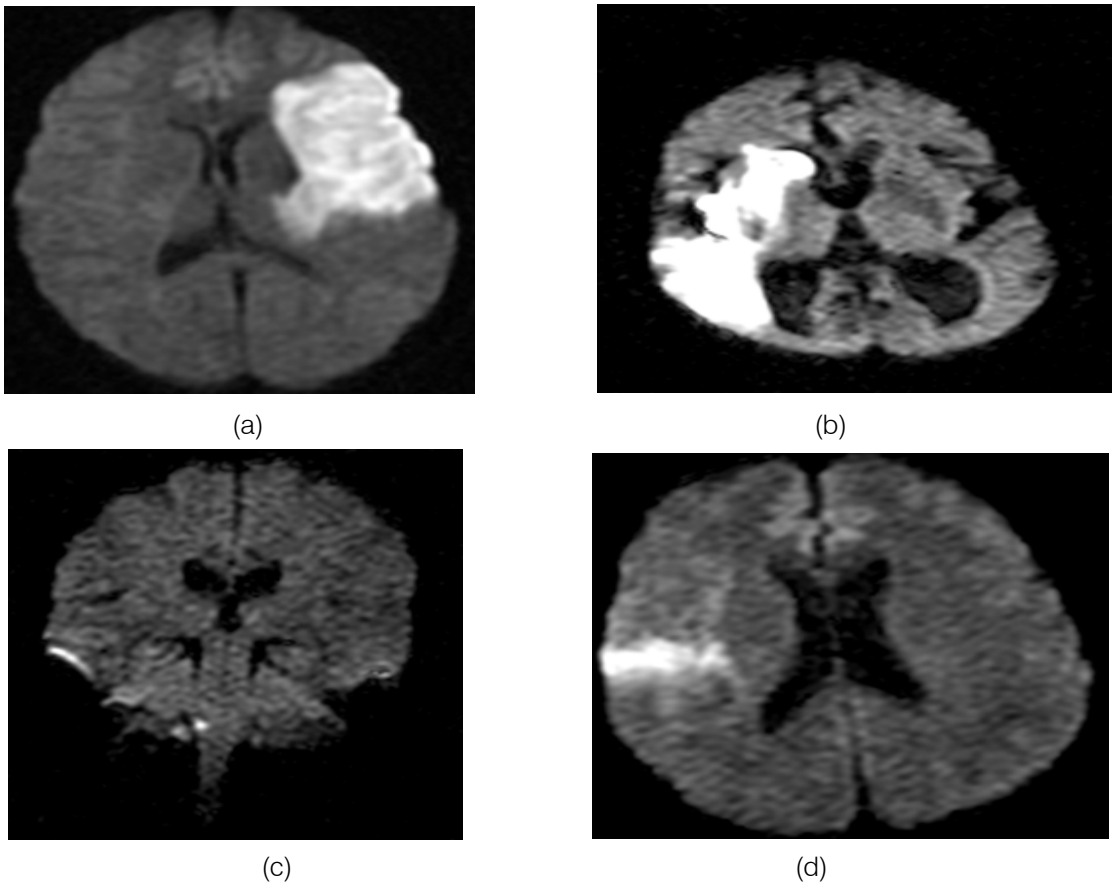
Table 4: Description of ischemic stroke subtypes according to "TOAST" classification of acute ischemic stroke among study cases

		N	%
Stroke subtype	Small vessel occlusion(lacunae)	243	54.4%
	Large artery atherosclerosis	143	32.0%
	Undetermined etiology	40	8.9%
	Cardioembolic	18	4.0%
	other determined etiology	3	.7%

Table (4) shows that subtype of acute ischemic stroke among 447 patients of study cases were classified according to "TOAST" criteria into (Figure 1):

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1) Small vessel disease (lacunar) stroke 54.4 %.
2) Large artery atherosclerosis (thrombosis-embolism) 32.0 %.
3) Cardio embolic stroke 4.0 %.
4) Stroke of undetermined etiology 8.9%.
5) Other determined etiology stroke (vasculitis due to collagen disease) 0.7%.



(a) (b) (c) (d)

a) Cardio embolic stroke
b) Large artery (RT ICA) atherosclerosis
c) lacunar stroke
d) Stroke of undetermined etiology

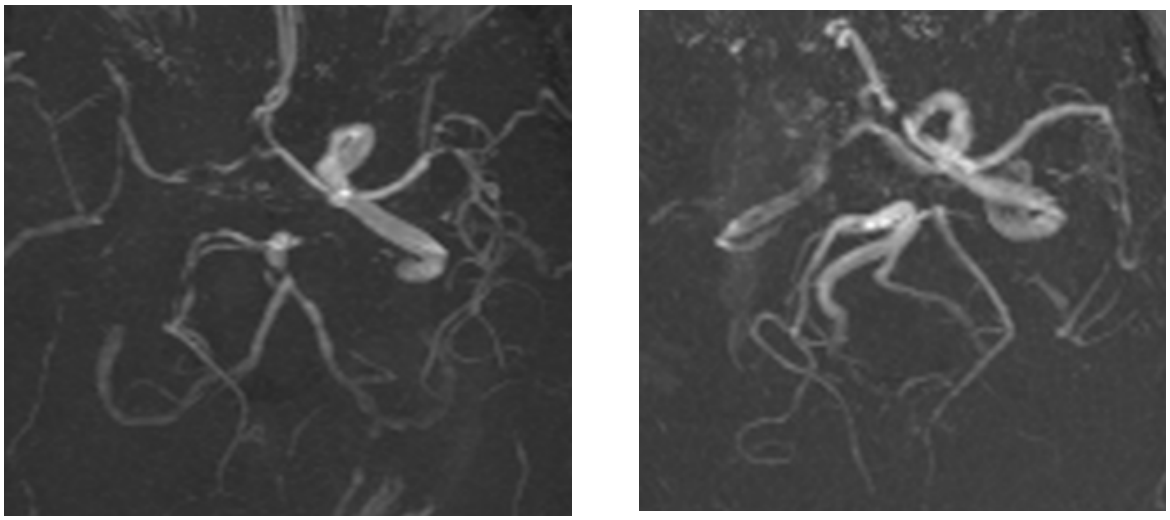
Figure 1: MRI Brain (DWI) showing different subtypes of acute ischemic strokes

Table 5: Description of presence of IC large vessel stenosis by TOF MRA Collapsed image among study cases

		N	%
Collapsed image MRA / Patient	Patent	111	35.4%
	<50% stenosis	86	27.4%
	>50% stenosis	72	22.9%
	Total occlusion	45	14.3%

Table (5) shows that (35.4%) of the study cases showed patent IC large vessels by TOF MRA. (27.4%) of study cases showed IC large vessel with <50% stenosis. (22.9%) of study cases showed IC large vessel with >50% stenosis. And (14.3%) of cases showed totally occluded IC large vessel (Figure 2).

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(A) (B)

A. Totally occluded RT. ICA, <50% stenosis of the RT. MCA and the Basilar A.
B. >50% stenosis of the RT. ICA and totally occluded RT. MCA.

Figure 2: Intracranial large vessel stenosis and occlusion by TOF MRA (Collapsed image) of the Ant. and Post. Circulations

IV. Discussion

Although epidemiologic studies on stroke were carried out in different parts of the world including some neighboring Arab countries, there were no published data from Egypt.[5]

This study revealed that the mean age of study cases was (63±10.9 years). Males represented (67.1%) of study cases. our results were close to thirty one articles reviewed from different Arab countries.[5]

All studies except two found stroke more commonly in males than females (range for males 55.9–75%).[5] One study from Saudi Arabia showed an equal ratio of males to females and another from Kuwait showed a slightly higher female preponderance at 51.7%.[9] The incidence of stroke, as expected, increased with age.[5]

This study revealed that (95%) of the study cases were ischemic strokes, while (5%) of study cases were hemorrhagic strokes (all were intracerebral hemorrhage). Our results showed higher incidence of ischemic strokes in comparison to Arab countries, in which ischemic stroke was the commonest type in all series, ranging from 55–87%, while cerebral hemorrhage occurred in 6.3–41. 3% and subarachnoid hemorrhage in 1–9%.[5]

This study revealed that subtypes of acute ischemic stroke among cases were classified according to "TOAST" criteria into: Small vessel disease (lacunar strokes) (54.4%), Large artery atherosclerosis (32.0%), Cardio embolic strokes (4.0%), strokes of undetermined etiology (8.9%) and strokes of other determined etiology i.e. vasculitis due to collagen disease (0.7%). Regarding Arab countries, Non-lacunar infarction represented 33–65.5% of strokes while lacunar infarction was reported in 10–35% of patients.[5] these results emphasize our finding of the higher preponderance of lacunar infarction among current study cases (54.4%).

This study revealed that the most prevalent risk factor for stroke among cases was HTN (70.1%), followed by DM (53%), and Heart diseases (35.4%) with "ISHD representing (22%), AF (5.9%), and MI (1.4%), PH of stroke was present among (30.4%) of study cases. Smoking (25.7%).

Hyperlipidemia was present among (8.9%) of study cases, while PH of TIAs was found among (8.7%) of study cases, PH of cerebral hemorrhage among (2.4%) of cases, and alcohol consumption (0.4%). Regarding Arab countries, HTN was the most frequent risk factor among stroke patients, being present in 24.9–76% of reported patients, followed by DM which was present in 11.6–69.4%. Hyperlipidemia was reported in 4–61% of patients. And other risk factors were as follows: cardiac disease 5–50%, cigarette smoking 1.6–44%, and previous transient ischemic attack 2.1–46%. [5] these results came in concomitant with our findings of the higher prevalence of HTN and DM.

This study revealed that (35.4%) of the study cases showed patent IC large vessels by TOF MRA collapsed image, while (64.6%) of the study cases showed stenotic and occluded IC large vessels as follows: (27.4%) of study cases showed IC large vessel with <50% stenosis, while (22.9%) of study cases showed IC large vessel with >50% stenosis. And (14.3%) of cases showed totally occluded IC large vessel.

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These results emphasized findings of previous many studies in populations of Asian, African, and Hispanic descent that demonstrate the preponderance of intracranial stenosis compared with extra cranial carotid stenosis.[10] In contrary to the developed world, in which imaging research has largely focused on extra cranial atherosclerosis, with lower incidence of intracranial stenosis in its white population.[11]Asubstantial study of 300 stroke fatalities in Paris showed that intracranial atherosclerotic plaque occurred in 59% of patients and 37.2% of all patients had intracranial plaque that was stenotic.[10,12]

V. Conclusion

Ischemic stroke is the most prevalent type of stroke (95%), Lacunar stroke (54.4%) is the most prevalent ischemic stroke subtype, HTN (70.1%)is the most prevalent risk factor for stroke. IC large vessel stenosis was prevalent among (64.6%) of study cases.

VI. Recommendations

Effective primary and secondary prevention of stroke would not be possible without a thorough understanding of the relevant risk factors and stroke subtype.MRA Brain is an important investigative tool for detection and estimation of intracranial (IC) large vessel stenosis which represents a challenging and important clinical situation in everyday neurology practice especially among stroke specialists.

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Neuro form EZ Stent for Late Thrombosis after Carotid Intracranial Stenosis: A Case Report and Literature Review

By Bin Liao, Huanlun He, Liang Zhang, Kaifeng Li, Xiongjun He & Yajie Liu

Introduction- The patient was a 44-year-old male. He came to Fenggang People's Hospital in Dongguan City, Guangdong Province for left limb weakness in November 2019. His NIHSS score on admission was 1 point. The diagnosis was as follows: 1. acute watershed infarctions in the bilateral cerebral hemispheres; 2. occlusion of the right internal carotid artery (segment C6) and left internal carotid artery; 3. hyperlipidaemia; 4. prior bilateral occipital lobe old cerebral infarction, treated with aspirin 100 mg qd and atorvastatin 40 mg qn. Following the treatment of the previous infarction, the patient's symptoms had improved, and he had been discharged with an NIHSS score of 0 points.

Keywords: stent; thrombosis; intracranial artery stenosis.

GJMR-A Classification: NLMC Code: WL 340

NEURODFORMEZSTENTFORLATETHROMBOSISAFTERCAROTIDINTRACRANIALSTENOSISACASEREPORTANDLITERATUREREVIEW

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Neuro form EZ Stent for Late Thrombosis after Carotid Intracranial Stenosis: A Case Report and Literature Review

Bin Liao [α], Huanlun He [σ], Liang Zhang [ρ], Kaifeng Li [ω], Xiongjun He [¥] & Yajie Liu [§]

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I. Introduction

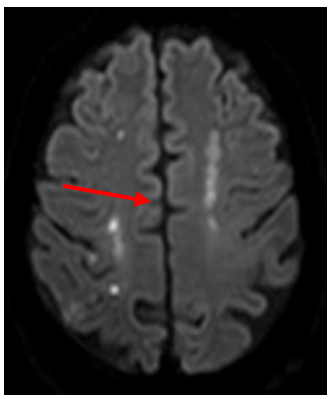
The patient was a 44-year-old male. He came to Fenggang People's Hospital in Dongguan City, Guangdong Province for left limb weakness in November 2019. His NIHSS score on admission was 1 point. The diagnosis was as follows: 1. acute watershed infarctions in the bilateral cerebral hemispheres; 2. occlusion of the right internal carotid artery (segment C6) and left internal carotid artery; 3. hyperlipidaemia; 4. prior bilateral occipital lobe old cerebral infarction, treated with aspirin 100 mg qd and atorvastatin 40 mg qn. Following the treatment of the previous infarction, the patient's symptoms had improved, and he had been discharged with an NIHSS score of 0 points. After discharge, he regularly took "aspirin 100 mg qd, atorvastatin calcium tablets 10 mg qn". On December 3, 2019, the left limb was numb and fatigued, and the patient's speech became ambiguous again. Then, he came to the Department of Encephalology, Dongguan Traditional Chinese Medicine Hospital, Guangzhou University of Traditional Chinese Medicine. Head and neck magnetic resonance imaging showed multiple small frontal parietal infarcts (Figure 1); bilateral occipital lobe, left thalamus, and right cerebellar hemisphere softening; left anterior cerebral and middle cerebral arteriosclerosis, mild to moderate stenosis; occlusion throughout the left internal carotid artery and in the bed of the upper right carotid artery; and severe stenosis at the end of the right carotid artery. DSA showed severe stenosis of the upper part of the right carotid artery bed and occlusion at the beginning of the left internal carotid artery (Figures 2a, 2b). After admission, he was treated with aspirin 100 mg qd, clopidogrel sulfate 75 mg qd, atorvastatin 40 mg qn, and butylphthalide capsules 0.2 g tid. After treatment, his limb weakness improved, and he was discharged. His NIHSS score at discharge was 0 points. After discharge, the patient was treated with "aspirin 100 mg qd, clopidogrel sulfate 75 mg qd, and atorvastatin 40 mg qn. On January 13, 2020, became to our hospital again for further endovascular treatment. High-resolution magnetic resonance imaging was performed, revealing that the upper segment of the right carotid artery bed was severely narrowed (ulcerous plaque) (Figure 3) and that the left internal carotid artery was occluded. Genotyping of clopidogrel response genes detected an intermediate metabotype. After communicating with the clinical team, the patient and family members agreed to surgery.

On January 15, the patient underwent balloon dilation and stenting of the right carotid artery under general anaesthesia. After successful puncture of the right femoral artery, systemic heparinization was performed (calculated based on 2/3 of body weight, that is, 0.667 mg per kilogram of body weight plus 1/2 of the previous dose per hour until 10 mg). A 6 F guide catheter was placed in the C1 segment of the right internal carotid artery (Figure 4). Under roadmap guidance, a Tran send micro-guide wire measuring 0.014 * 205 mm (Boston Scientific Corporation, Stryker (Beijing) Medical Devices Co., Ltd.) was carefully transferred through the narrow section to the M1 segment of the right middle cerebral artery. A 3.0 * 15 mm NC TREK RX coronary balloon (Abbott Vascular, USA) was selected and placed in the stenotic section under the guidance of a microwire. After accurate positioning, the stenosis was slowly expanded at 8 standard atmospheres of pressure (Figure 5a). After the stenosis was slowly expanded further at 10 standard atmospheres of pressure, the local dissection and elastic retraction were observed on angiography (Figure 5b). A Neuro form EZ (4.5 * 20 mm, Stryker (Beijing) Medical Devices Co., Ltd., Stryker Neurovascular, USA) stent was passed through the stenosis, and the stent was released after positioning. The angiography showed that the stent was well positioned, the stenosis was improved, and the residual stenosis was approximately 30%. The patient's m TICI classification was Level 3 (Figure 6). The patient's vital signs were stable after the operation, the left limb could be lifted, the NIHSS score was 0, and the postoperative blood pressure was controlled at 100-140/60-90 mmHg; he was prescribed aspirin 100 mg qd, clopidogrel sulfate 75 mg qd, and atorvastatin tablets 40 mg qn. At 21:00 on the night of the operation, the patient's left limb muscle activity was good. At 7:30 the next morning (approximately 15 hours after surgery), the patient was mentally exhausted, his speech was unclear, the muscle strength of the left limb was decreased, the muscle strength of the left upper limb was grade 0, and the muscle strength of the left

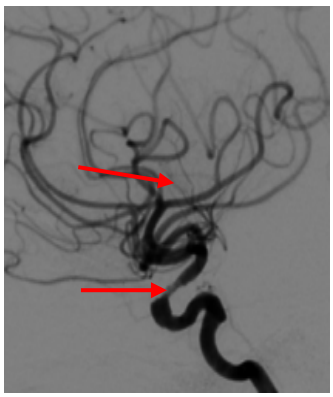
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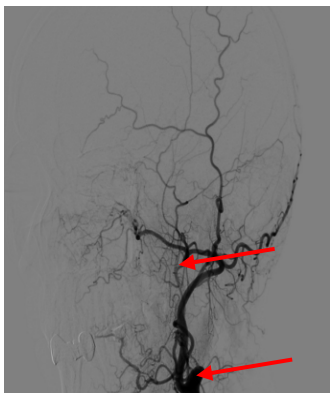
lower limb was grade 4. The patient's NIHSS score was 6 points. A rapid MRI of the head to examine the right frontal and parietal lobes revealed multiple new infarcts in the bilateral frontal and parietal cortex (Figure 7a). Skull MRA showed bilateral internal carotid artery occlusion (Figure 7b), bilateral anterior and middle cerebral arteriosclerosis, and mild to moderate stenosis of the lumen. The patient had multiple recent infarcts in the right frontal parietal cortex and subcortex. Internal carotid artery occlusion caused by an embolization event or stent thrombosis was considered likely. Given the uncertainty of the patient's limb muscle strength, the infarct size was inferred to be large, and he was not eligible for intravenous thrombolysis because his last normal time had been 15 hours prior. The area of the cerebral infarction was large, and the risk of thromboem bolism and bleeding after revascularization was high. The patient's family members did not agree to repeated intravascular treatment, and he continued to receive stroke prevention, dehydration, cranial pressure, collateral circulation, and active acupuncture rehabilitation treatment. A review of head and neck CTA during treatment showed that the bilateral internal carotid artery was occluded, the distal end of the stent was well developed, no blood flow was visible at the proximal end of the stent, and a thrombus had formed at the proximal end of the stent (Figures 8-11). After treatment, the patient's left upper limb muscle strength recovered more than before, reaching grade 3 proximally and grade 1 distally; the left lower limb muscle strength was grade 5 both proximally and distally. The patient's NIHSS score on discharge was 3 points.



▪ 4



▪ 2a



▪ 5a

▪ 2b

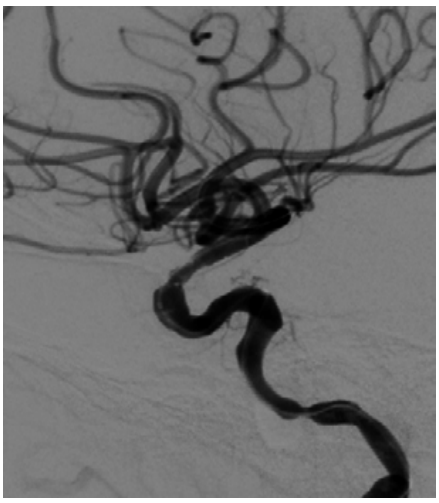


▪ 5b

▪ 3



▪ 6

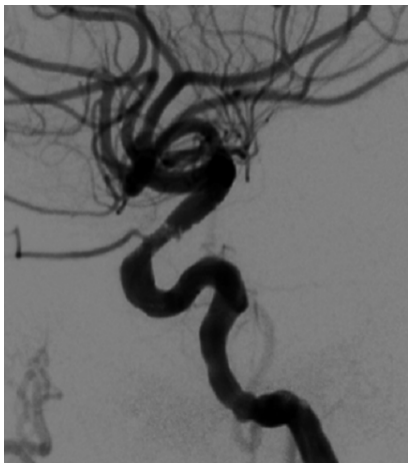


▪ 7a

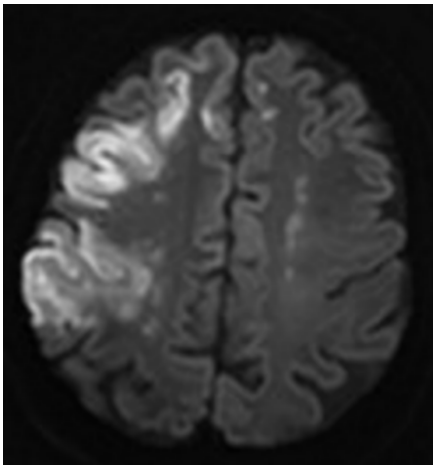


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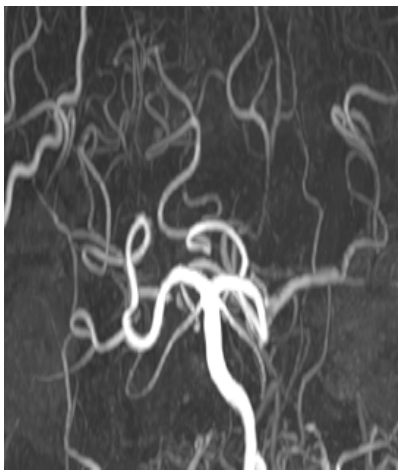
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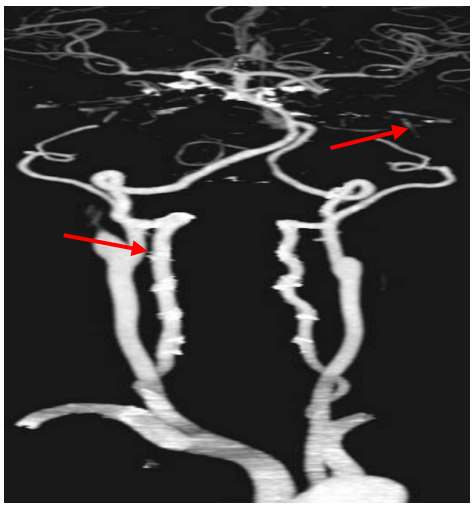
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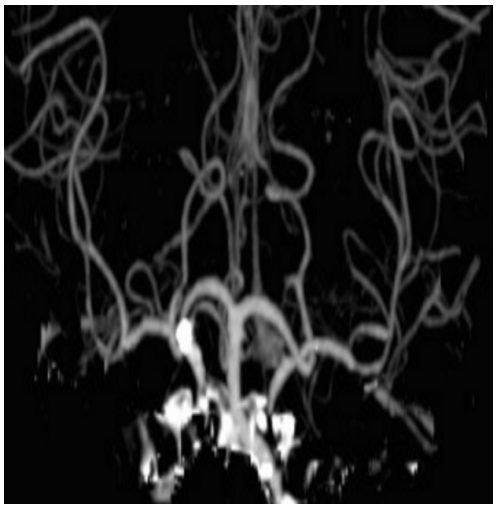
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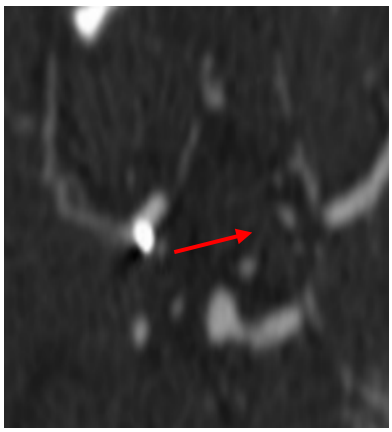


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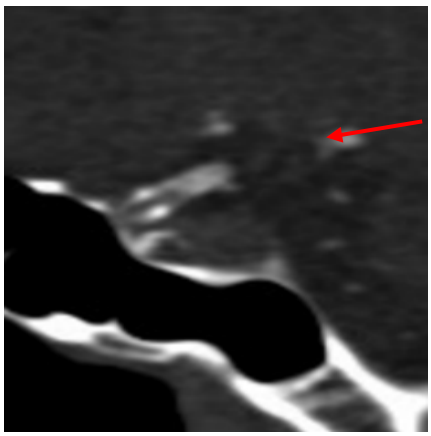


▪ 8

▪ 9



▪ 10



▪ 11

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Note: figure 1: Multiple small frontal parietal infarcts; Figure 2a: Severe stenosis of the upper part of the right carotid artery bed; Figure 2b: 0cclusion at the beginning of the left internal carotid artery; Figure 3: The upper segment of the right carotid artery bed was severely narrowed (ulcerous plaque) ; figure4-6(surgical procedure):Figure 4: A 6 F guide catheter was placed in the C1 segment of the right internal carotid artery; Figure 5a: The stenosis was slowly expanded at 8 standard atmospheres of pressure; Figure 5b: After the stenosis was slowly expanded further at 10 standard atmospheres of pressure, the local dissection and elastic retraction were observed on angiography; Figure 6: The patient's m TICI classification was Level 3; Figure 7a: 15 hours after operation, a rapid MRI of the head to examine the right frontal and parietal lobes revealed multiple new infarcts in the bilateral frontal and parietal cortex; Figure 7b: Bilateral internal carotid artery occlusion; Figure 8-11: A review of head and neck CTA during treatment showed that the bilateral internal carotid artery was occluded, the distal end of the stent was well developed, no blood flow was visible at the proximal end of the stent, and a thrombus had formed at the proximal end of the stent.

II. Discussion

Ischaemic cerebro vascular disease is a common disease in neurology, and angioplasty has become a treatment option. Endovascular treatment of symptomatic severe intracranial arterial stenosis has been used in clinical practice. Compared with drug treatment alone, interventional therapy can improve and restore the shape and blood flow of intracranial arteries, stabilize plaque, and reduce the long-term incidence of stroke [1]. Acute stent thrombosis is one of the rare serious complications of intracranial arterial stenting. According to the time of occurrence, it can be classified as early, delayed, or very delayed. Early intra-stent thrombosis, defined as occurring within 30 days after PCI, includes acute (24 hours after PCI) and sub acute (24 hours to 30 days after PCI) intra-stent thrombosis. Delayed intra-stent thrombosis is defined as occurring 30 days to 1 year after PCI, and very delayed intra-stent thrombosis is defined as occurring more than 1 year after PCI [2]. By reviewing the relevant literature and combining the clinical data of this patient, we analysed the common factors of stent thrombosis, including plaque rupture, platelet activation, increased release of procoagulant substances in the body, hypercoagulable state, insufficient anti platelet aggregation treatment, clopidogrel or heparin resistance, thinned blood vessels, long lesions, diabetes, chronic renal insufficiency, poor stent and blood vessel fitting, and excessive stent placement.

a) Anatomical characteristics of the siphon of the internal carotid artery

The formation and progression of internal carotid artery stenosis is complicated by the interaction of systemic factors, changes in the biomechanical properties of the vessel wall, and local haemodynamic factors (such as low and oscillating wall shear stress) [3, 4]. Arterial stenosis often occurs in areas related to changes in blood flow, such as bends and bifurcations [5]. The internal carotid artery siphon section is noted for its tortuosity and is among the sites most sensitive to vascular injury [6]. Studies have shown that the geometry of the internal carotid artery plays an important role in the occurrence and development of stenosis. A new classification of "U", "V", "C" and "S" shapes of carotid siphons has been proposed. There is a correlation between stenosis and morphological classification of the siphon. Haemodynamic simulation results for the siphon showed that different haemodynamic factors have different distribution rules among different types of internal carotid arteries, which verified the influence of internal carotid artery geometry on haemodynamics and stenosis. According to clinical reports, stenosis mostly occurs in the second half of the C2 segment and in the full C4 segment [7, 8]. In the siphon, U-shaped morphology is the most common type. In a comparison of the stenotic parts of the siphon section, there was no significant difference in the incidence of C2-segment stenosis among different morphologies, whereas U-shaped siphons were significantly more likely than other morphologies to have C4-segment stenosis. In addition, a U-shaped internal carotid artery may have more stenoses than other morphologies, and there is a higher risk of atherosclerotic stenosis. There may be an increased risk of restenosis after stenting. The patient's siphon was tortuous and "U"-shaped. The proximal end of the stent was at the genu, and the distal end was at MCA M1. The lesion was narrow and severe, and the two ends of the stent were bent. The radial force of the lesion failed to reach the maximum, and the stent adheres poorly, which posed a high risk of intra-stent thrombus formation and a high risk of restenosis after surgery.

b) The characteristics of stenotic lesions

1) The patient's lesion was an unstable plaque, and high-resolution magnetic resonance imaging revealed a thin fibrous cap and many lipid cores. No obvious calcified plaque was seen. After balloon dilatation and stent formation, the plaque was easily ruptured and displaced, the degree of intimal avulsion was intensified, and the thrombus-forming substance was exposed under the in tima. Partially displaced plaques and avulsed endometrium could still penetrate the gap of the stent, increasing the risk of thrombosis and plaque detachment.

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2) Regarding the geometric and structural features of intracranial blood vessels, Mori et al. [9] defined 3 types (A, B, and C) of stenotic intracranial vessels. The structure of type a vessels is relatively simple, and the incidence of acute thrombosis and restenosis after angioplasty is relatively low. Types B and C vessels are at an angle, and the thrombus is eccentric. After angioplasty, the blood vessels change greatly, and the changes in blood flow are complicated. The rate of acute thrombosis and restenosis after operation is relatively high. In this case, high-resolution magnetic resonance imaging showed severe stenosis caused by a partial plaque. The angiography showed that the length of the stenosis was less than 10 mm, and it was classified as type B. This was one of the factors that caused acute thrombosis and restenosis after surgery.
3) Following angioplasty, the structural characteristics of intracranial blood vessels change in a different manner from those of coronary arteries. The outer wall of intracranial blood vessels is thin, the muscle layer is discontinuous, and cerebral effusion readily infiltrates. The potential damage may cause the destruction of vascular integrity, which, in turn, leads to acute thrombosis after surgery through a series of coagulation mechanisms [10].

c) The details of the operation

1) Local observation of lesions during surgical release of the stent showed that the stent was not smooth and had residual stenosis (30%); the mTICI classification was grade 3. After 20 minutes of observation, the stent, localized in the lesion, was not smooth, and there was a possibility of local thrombosis, which was one of the factors that promoted thrombosis in the stent.
2) After the intraoperative guidance was in place, the diseased blood vessels spasmed, the siphon section became more curved, and the blood flow rate was slowed. This was one of the factors that caused thrombosis. The patient's intraoperative vasospasms were caused by mechanical stimulation from the 6 F guide wire. The blood vessels were still contracted after the stent was released, and the spasm was relieved after the stimulation was reduced and intravenous papaverine was administered.

d) Material selection

1) A balloon measuring approximately 3.0 * 15 mm was used during surgery to cover the lesion. At the first dilation, the pressure was 8 atm. After dilatation, the degree of stenosis was improved (Figure 5a), but the residual stenosis was increased. The second expansion was performed with a pressure of 10 atm. After the expansion, the stenosis showed elastic retraction, and the local dissection appeared (Figure 5b). There may have been insufficient pre-expansion, increasing the residual stenosis rate and poor adherence after stent release. A meta-analysis of the literature shows that the use of intravascular ultrasound during coronary stent implantation can guide the stent to completely adhere to the wall, thereby greatly reducing the incidence of acute stent thrombosis and providing a reference for intracranial stent surgery [11]. A study showed that a stent diameter/vessel diameter ratio (SAR) of 1.2 or less yielded good results. When the SAR is greater than 2, it can cause immediate vasospasm, immediate and delayed thrombosis, and intimal hyperplasia [12]. During surgery, the diameter of the distal end of the blood vessel was 3.8 mm. The diameter of the stent was 4.5 mm, and the length was 20 mm. The lesion was completely covered. The atherosclerotic artery plaque that was cut near the distal and distal edges of the stent was not considered to cause thrombosis. In percutaneous coronary angioplasty (PTCA), when the stent diameter is greater than 3 mm and the SAR is greater than 1, the restenosis rate is significantly reduced after stent placement. Anticoagulation needs to be increased after stent placement in small and low-flow vessels, and platelet aggregation should be inhibited for at least 8 weeks [13].
2) Current stents for intracranial atherosclerosis include the Wingspan and Apollo stents. The Wingspan stent is an open-loop self-expanding stent, which has higher adherence to tortuous blood vessels and a stronger radial support force than the Apollo stent, but the former is more difficult to place, and the operation is more complicated after release. The Apollo is a balloon-expandable stent that can be positioned accurately but is difficult to pass through a tortuous lesion, and it is also prone to displacement. The maximum diameter is 4.0 mm. In cases such as ours, a small stent can cause poor adherence and a high restenosis rate. The Neuro form EZ stent is an open-loop design and has superior adhesion to tortuous vascular segments. The patient had a tortuous "U"-shaped siphon. Nonetheless, the micro catheter release stent easily reached the lesion, and the release was simple. In the current case, we considered the options and chose to implant a Neuro form stent, but in cases where it is difficult for a stent to support the siphon segment, the intervention is difficult, and there are certain risks and challenges in balloon expansion and stent implantation.
3) The Neuro form EZ is an auxiliary intracranial aneurysm stent. Among four available auxiliary aneurysm stents, the radial support force is as follows: the LVIS stent has the highest supporting radial force (37.1 gf), followed by the Leo stent

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(34.2gf), Enterprise stent (15.2 gf), and Neuroform stent (11.4 gf). Krischek's study [14] and other works compared the radial force of the self-expanding Wingspan stent and the Enterprise, Solitaire, Neuroform, and Leo auxiliary aneurysm stents at 50% compression, and there was a clear ranking of radial strength, which, from lowest to highest, was as follows: Leo, Neuroform3, Enterprise, Solitaire, and Wingspan. The support of the Neuroform stent is weaker than that of the previous three stents. Several stent comparisons showed that the Neuro form had relatively weak radial force. After treatment of severe stenosis in the present case, there was severe residual stenosis, which can easily lead to stent thrombosis. In addition, the siphon lesion was tortuous. The proximal end of the stent was in the genu, and the distal end was in MCA M1. The lesion was narrow and heavy, and the two ends of the stent were curved to the maximal extent.

4) The mesh area of the Neuroform stent is larger. The Leo and LVIS stents (0.979 and 0.782 pores/mm2, respectively) have higher pore density than the Neuroform and Enterprise stents (both 0.276 pores/mm2, respectively). The lesions in patients with stenosis are mainly ulcerated plaques. When the stent mesh is large, the plaques can easily rupture and cause irritation at the site of their adhesion to the stent. This is one of the factors causing intra-stent thrombosis.

e) Postoperative Medication

Strict anti platelet therapy before surgery is an important factor in preventing stent thrombosis. Preoperative regular oral aspirin 100 mg qd and Polivir 75 mg qd were used for 20 days, and this preparatory drug regimen was not considered insufficient. Acute and sub acute thrombosis in the stent is mostly resistant to anticoagulant and anti platelet aggregation drugs [15]. Gene polymorphisms such as CYP2C19, CYP2C9 and CYP2B6 are closely related to clopidogrel resistance. Patients with CYP2C19 allele mutations are prone to clopidogrel resistance, and the incidence of cardiovascular is chaemic events and mortality is increased [16]. Xie et al. [17] showed that weak clopidogrel metabolism is an independent predictor of stent thrombosis within 1 year after PCI. Testing of clopidogrel metabolism genes in the present patient suggested an intermediate metabo type, which may be related to clopidogrel resistance. The doses of drugs such as ticagrelor or cilostazol can be adjusted based on clinical outcomes. Postoperative anticoagulation treatment can reduce or eliminate the risk of stent thrombosis. The absence of anticoagulant therapy after surgery may increase the risk of stent thrombosis.

f) Postoperative observation

At 21:00 the day after surgery, the patient's left limbs were flexible, but his left limb movement was poor after he woke up the next day. His symptoms had worsened in that 10-hour period. Magnetic resonance imaging showed a large area of cerebral infarction, and the right internal carotid artery was occluded. Because of the high risk of recanalization bleeding, interventional recanalization was not performed at that time. By strictly observing patients' neurological symptoms during sleep, it is possible to detect the functional deficits of patients early and make time for recanalization and saving of nerve function. Strict blood pressure management is an important measure during the perioperative period. High blood pressure can lead to hyper perfusion syndrome and even cerebral haemorrhage. Low blood pressure can lead to insufficient cerebral perfusion and cerebral infarction. The postoperative blood pressure of our patient was strictly controlled at 100-140/60-90 mmHg.

III. Conclusion

The efficacy of intracranial angioplasty has been affirmed, but the serious complication of late thrombosis after angioplasty is an important risk that should be given sufficient attention. For internal carotid artery stent implantation, pre-expansion must be sufficient. A stent with good support must be selected. The release of the stent through a micro catheter may increase the risk of thrombosis in the stent and should be performed with caution.

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Validation of Psychoactive Substance Dependence

By D. G. Baitubayev & M. D. Baitubayeva
Semey State Medical University

Summary- The article shows that the current level of physiology does not explain the biological mechanisms of the organism transition from one adaptation range to a higher one, with an increase in the strength of the regular stimulus above the sub-extreme level. A new trend in the physiology of adaptation - proqredient adaptation - explains the mechanism of increasing the resistance of the organism with dependence on psychoactive substances (PAS). It is scientifically proved, that dependence of the organism on PAS is not the disease, but the state of proqredient adaptation.

Keywords: hypertrophy of the endocrine system, proqredient adaptation.

GJMR-A Classification: NLMC Code: WS 107

VALIDATIONOFPSYCHOACTIVESUBSTANCEDEPENDENCE

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Validation of Psychoactive Substance Dependence

D. G. Baitubayev [α] & M. D. Baitubayeva [σ]

Summary- The article shows that the current level of physiology does not explain the biological mechanisms of the organism transition from one adaptation range to a higher one, with an increase in the strength of the regular stimulus above the sub-extreme level. A new trend in the physiology of adaptation - proqredient adaptation - explains the mechanism of increasing the resistance of the organism with dependence on psychoactive substances (PAS). It is scientifically proved, that dependence of the organism on PAS is not the disease, but the state of proqredient adaptation.

Keywords: hypertrophy of the endocrine system, proqredient adaptation.

I. Urgency of the Issue

It is known, that at the peak of dependence on any psychoactive substances (PAS), a person, for example, an opium (heroin) addict, uses doses, which are multiple times, almost 10 times, higher than the lethal dose for an ordinary person [3, p.23].

The fact that the drug user does not die is explained by the increase in the body's tolerance in response to the increase in the dose of PAS [3, p.25].

But urgent issues of medicine are not only disclosure of the mechanisms of increasing tolerance , but also validation of the physiological process occurring under the influence of increasing doses of psychoactive substance and the responsive increase in the body tolerance in PAS dependence.

Purpose and objectives of the study: Adaptive responses of the organism under regular exposure to a sub-extreme stimulus. Lack of adaptive responses of the body already known in physiology to explain the adaptation mechanisms in response to a further increase in the regular stimulus strength above the sub-extreme level in PAS dependent patients.

The pronounced responses by the vegetative nervous system (VNS) in PAS dependent patients indicate the vegetotrophy of most of these substances. Power of their influence is closest to the sub-extreme level. Responsive adaptive reactions of the organism under regular influence of the external factor of the average to sub-extreme strength were studied by L. Kh. Garkavi and co-authors (1977) [4, p.77]: Under the influence of sub-extreme stimuli, an activation reaction with the stages of primary and persistent activation is produced, indicating a higher activity of protective systems. The stage of persistent activation is true active resistance, which is stable and long enough-up to six months-in contrast to the training reaction and in the absence of constant exposure [4, p.79]

But in PAS dependence, the process does not result in the reaction of persistent activation; the dose to which the adaptation has been produced is habitual and results in no euphorizing effect.

To achieve neurophysiological shift sufficient for euphoria, a large dose is required.

But increase in the dose of PAS after the activation reaction is stressful for the organism. Stress in its development has three stages.

The first stage is the "anxiety reaction", the second one is the stage of resistance, when hypertrophy of the adrenal cortex with a steady increase in the formation and secretion of corticosteroids develops. They increase the amount of circulating blood and blood pressure, have an antihistamine effect, enhance gluconeogenesis, normalize physiological response, etc. The resistance of the organism to the stimulus increases. Prolonged exposure to the stimulus results in the stage of exhaustion, and death may occur. Doses of PAS above the stress level are lethal [1].

L. Kh. Garkavi and co-authors showed that: "the reactivity of the organism is represented by a number of floors (ranges), which does not exceed ten. In each floor: a weak stimulus causes the training reaction, an average sub-extreme stimulus - the activation reaction, a strong stimulus – the stress. The ranges are separated by the zone of non-reactivity, when increasing the stimulus level above the stress one or decreasing below the training one causes no reaction. Transition to the next range shows again the same order of reactivity: the reactions of training, activation, and stress [4, p.77].

But L. Kh. Garkavi and co-authors could not explain the mechanisms providing non-fatal transition of the organism from one floor (range) of adaptation to a higher one, after the reaction of primary and persistent activation and further enhancement of the effect above the sub-extreme, stress and higher levels.

Indeed, according to pathophysiology, without such adaptation mechanisms increasing the resistance,

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the body must die from "exhaustion", from failure of adaptation mechanisms, when the organism transits from the first adaptation range to the second. But this is not observed in a PAS dependent people. This indicates failure of the current level of physiology to explain the mechanisms providing the body transition from one adaptation range to a higher one.

In the history of narcology, attempts were made to explain the increase in tolerance and the accelerated disintegration of PAS in the addict's organism by different causes. They are the occurrence of the state of chronic stress, activation of other states inactive in normal conditions or activation of systems that fulfill other functions, but with an increase in a PAS dose are forcedly involved in detoxification, etc. But all those assumptions have not been scientifically confirmed.

No matter how full modern scientific research explain qualitative changes at the cellular and molecular level that lead to an increase in tolerance in PAS dependent patients, it is clear that these changes can only be of adaptive, not pathological and damaging nature, otherwise they would lead not to an increase in tolerance, but rather to a decrease in it, and the body would die since transition from the first floor of adaptation to the second. Also, according to the dialectical principle of the mutual transition of qualitative changes to quantitative ones, accumulation of these changes should lead to qualitative and quantitative changes in the neuroendocrine system which is responsible for the adaptation of the whole organism.

I would like to quote L.Kh. Garkavi, E.B. Kvakina, M. A. Ukolova (1977) - "it is possible to investigate separately the changes in any one system or at any one level, for example, molecular. But this is only a part of the changes in the overall complex reaction of the body. "Also I would like to quote I.N. Pyatnitskaya (1988):

> "Integral functional reactions to the intoxication of physiological systems are known to be no less important in maintaining homeostasis than biochemical protection" [5, p.58]. Consequently, we can speak about change of the body's response to a drug. "
>
> Object and methods of investigation: Features of the response of the neuroendocrine system to any external stimulus. Capacity of the endocrine system for positive trophic changes. Hypertrophy and hyperfunction of the endocrine system are histological and biochemical evidence.

The response of the body to any change in the internal environment depends primarily on the functional state of the neuroendcrine system.

Thus, the reason of the altered reactivity of the organism and a steady increase in the overall tolerance of the organism, should be sought in the central mechanisms of adaptation - in the neuroendocrine system.

The increase in resistance of the PAS dependent organism can be explained by the functional tension of the neuroendcrine system and by the reaction of persistent activation only within one adaptation range. It is good health, physical activity, increased protective capacities of the body to various hazards - hypothermia, etc., which are clinically observed in the prodroma and possibly in the initial stage of alcohol dependence.

But neuroendcrine system tension and the reaction of persistent activation fail to explain the transition from a lower to a higher adaptation range under PAS exposure above sub-extreme level and its further increase! After all, in such a situation, the body must experience stress with exhaustion and death! This can only be explained by the transcendental functioning of the neuroendocrine system, which can be possible only due to its adaptive hypertrophy, in response to the regular exposure to the external factor. But is it possible? According to the theory of physiology of the development of interrelations between the structure and the function, in the course of ontogenesis (individual's development), functional activity is of particular importance and it is stimulated by the flow of stimuli affecting the organism as a result of changes in living conditions. Functional activity is the leading factor causing adaptive reactions in the body up to the development of morphological changes. Morphological changes occur in organs or systems stimulated by a flow of stimuli more regularly.

Even in the early 1800s, J. Lamarck suggested that "the work builds up the organs". P. Lesgaft's merit was the explanation of a specific morphological alteration of the organism during the exercise process. V.Ru showed that due to "trophic stimulation" in the working organ, the assimilation process begins to dominate over the dissimilation process, and morphological changes occur at the physiological level. The increase in energy reserves results in an increase in working efficiency.

It can be argued that the regular use of PAS-addressing the high response range-leads the entire body to the state of the activation reaction-hypermetabolic state, which does not contribute to the accumulation of reserves and the occurrence of positive trophic changes in the body. But one should remember that the hypermetabolic state develops in the "metabolic boiler" - at the level of tissue adaptation mechanisms [2, p.500]. Perhaps in the higher adaptation mechanisms - the neuroendocrine system - despite their tension, there are no hypermetabolization processes, which contributes to the accumulation of reserves leading to morphological changes in the neuroendocrine system in the form of hypertrophy, are there?

The observations of L.Kh. Garkavi and co-authors indirectly proves possible accumulation of

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reserves in the neuroendocrine system during the activation reaction; "Although the metabolism is highly active during the activation reaction, it is characterized by an equilibrium" [4, p.79], since to ensure "equilibrium" of constantly growing metabolic processes, a "powerful" neuroendocrine system is necessary.

But in PAS dependence, after the completion of the activation reaction and in further enhancement of the stimulus above the sub-extreme level and transition to the subsequent adaptation floor, the "equilibrium" of the metabolic processes takes place. But this is possible only when the functional adequacy of the neuroendocrine system grows in direct proportion to the strength of the external factor, which is possible only with hypertrophic neuroendocrine system and, as a consequence, its hyperproductivity.

Hypertrophy of neuroendocrine system is evolutionally provided by the functional mechanism contributing to the accumulation of reserves - "advanced excitation" described in the 1930s by P. K. Anokhin: VNS responds to any stimulus with a somewhat excessive neurotransmitter ejection, as if in anticipation of possible future high consumption. VNS through neurotransmitters activates auxiliary and tissue adaptation mechanisms, and due to excesses of neurotransmitter ejection "takes a break" for its own recovery trophic processes. Although the VNS regulates all the processes in the body, it has been established that there are biologically active substances produced by different cells of the organism that have a trophic effect on VNS itself. One of such substances is the nerve growth factor (NGF) - an insulin-like substance that stimulates the growth of sympathetic ganglia. NGF is produced in the salivary glands by the smooth muscle fibers of the walls of internal organs. Similarly, the adaptive-trophic effect on VNS is provided by neuropeptides: liberins, somatostatin, enkephalins, endorphins, bradykinin, neurotensin, cholecystokinin, ACTH fragments, oxytocin [5, p.251].

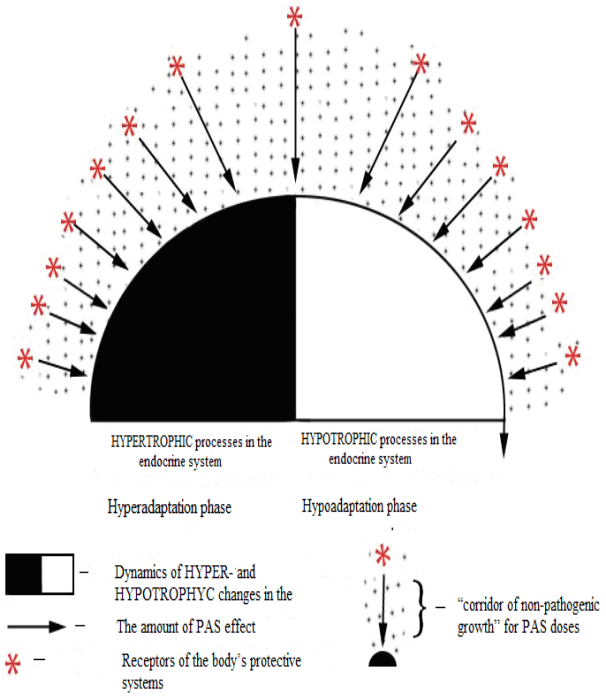
"When excited in neurons, metabolic processes are intensified, the amount of RNA increases, and the synthesis of proteins in neurons is enhanced. In neurons and glia cells surrounding them, these processes are multidirectional. RNA in nerve cells is increased due to the enhancement of its synthesis in a neuron and due to the transport of RNA from glial cells to neurons "[6, p. 250].

Histological evidence of the neuroendocrine system hypertrophy under regular exposure to a medium-strength stimulus is Selye's stress research: "adrenal glands bloom". But the adrenal medulla, which is a modified sympathetic ganglion. [2, p.525] can not be hypertrophied. Adaptive, positive, trophic changes, during pauses, allow the sympathetic ANS only to recover itself, not to be exhausted, to maintain productivity for a long time.Hypertrophy appertains to the structures. Therefore, speaking of adrenal hypertrophy, one should keep in mind the adrenal cortex.As early as in 1930s, it was found that chronic morphinization causes hypertrophy of the cortical layer of the adrenal glands in rats, which produces the "adaptation hormones" -glucocorticoids (hydrocortisone, cortisone and corticosterone), increasing the resistance of the organism to intensive stimuli [3, p. 260]. There is no doubt in the Adrenal cortex hypertrophy starts even in the activation reaction, since the process of adrenal hypertrophy is not spasmodic. There is no doubt that due to the mechanism of "advanced excitation", other internal secretion glands "takes a break" for trophic recovery processes, which leads to their hypertrophy and hyperfunctionality. Evidences of adaptive hypertrophy of the endocrine system are L. Kh. Garkavi and co-authors' observations under conditions of training and activation reactions – enlargement of not only the adrenal cortex, but also thymus gland, a prolonged increase in the thyroid and reproductive gland functions [4, p. 78].)

Results of the study and their discussion: Thus, under the regular exposure to PAS as a sub-extreme stimulus, while hypermetabolic processes occur in the "metabolic boiler," accumulation of reserves takes place in the neuroendocrine system, as a result of "advanced excitation". This accumulation of reserves leads to adaptive hypertrophy and hyperfunction of the endocrine system, which results in an increase in the general and specific resistance of the organism to a certain PAS.

That is why, a subsequent, increasing, potentially extreme dose of PAS has a sub-extreme non-pathogenic effect on the body. The condition persists for the further adaptation (see the figure below).

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Thus, in PAS dependence, in each range and in the transition to a higher adaptation range, one should speak not of the reaction dyad: activation and persistent activation, but of the reaction tetrad: activation, persistent activation, then stress with "anxiety reaction", and the stage of resistance. And the hypertrophy of the neuroendocrine system that has developed to this moment, does not allow development of the final stage of stress - exhaustion. With an increase in the dose of PAS and transition to another range, everything comes around. It is more correct to call such a process a state of not chronic, but regular, unfinished stress. Stress without the exhaustion stage, no matter how regular it is, cannot be considered as a disease. That allows the body to transit to a higher range of adaptation without death. It becomes clear that increased resistance in persistent activation reaction responding to regular sub-extreme exposure to PAS and the resistance stage in stress responding to the further regular exposure to an increasing dose of PAS are functional manifestations of adaptive hypertrophic changes in endocrine system.

This process is called progredient (or progressive) adaptation. Beliefs about the unity of form and function, the stereotyped thinking that "if changes in the body are acquired and irreversible, therefore, they are pathological," have led to the erroneous judgment that the body's dependencies on PAS should be considered as diseases. There is the expression "any disease is an adaptation." But the opposite statement that "any adaptation is a disease" in relation to PAS dependencies is inadmissible. It is because neither failure, lack of adaptive capabilities, necessity of compensation for the adaptive capabilities of the body at the expense of any tissues or body systems is observed, nor the disease develops resulted from hypertrophy of the endocrine system and its high adaptive sufficiency leading to an increase in general and specific resistance. Thus, the adaptive possibilities grow in direct proportion to the increase in the dose. The role of the receptors of the body's protective systems indicating possible overdose of PAS is also important (✱- in the figure), as well as the experience of narcotization.

Due to the vegetotrophic nature of PAS, in PAS dependencies, the mechanism of PAS action, in contrast to the disease, is also different. Common pathogenic factors – without pronounced vegetotrophy - cause damage at first, and only then a protective reaction of the organism develops. PAS, simultaneously or primarily, affect the receptors of VNS, which causes its timely or even advanced reaction to possible damage from the PAS effects. The increase in the exposure dose occurs through the "non-pathogenic corridor" - between the body's protective systems and the timely responding, hypertrophic endocrine system (see Fig.2). That is why the acquired biological changes in PAS dependence are only of adaptive nature. One should talk about adaptively changed reactivity, about the adaptive attraction to PAS or, conversely, about the readaptation - deprivation syndrome, about adaptively changed behavior, and so on.

In the final stage of the dependence (see figure), depletion of the adaptive capabilities of the organism, due to the hypotrophy of the endocrine

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system (the receptors of the protective systems indicate possible PAS overdose), leads to a parallel decrease in the dose of PAS that a person is able to adapt. The effect of PAS turns out to be sub-extreme again and pathology is not observed either.

Pathology in PAS dependence is an accompanying phenomenon.

The explanation of the increased resistance of the adaptive hypertrophy of the endocrine system does not contradict the development of biochemical theories of the euphoria etiology, explains the internal mechanism of clinical manifestations in PAS dependence.

Under alcohol exposure, when to achieve euphoria and acquire dependence, abuse with adaptive, qualitative or quantitative changes in the mechanisms responsible for the euphoria is required, the accompanying increase in tolerance can be explained by the neuroendocrine system hypertrophy.

Productivity of VNS in the first stage of alcohol dependence explain maintaining the body tone during the week intervals of sobriety, in the absence of alcohol stimulation.

Compensatory stress and production of neurotransmitters or residual neurotransmitter excess, due to VNS productivity, explains adrenergic tension and vegetative disorders in the alcohol withdrawal syndrome.

The productivity of the sympathetic part of VNS against the background of the gradual exhaustion of the parasympathetic department (adrenergic system is more resistant even in ontogenesis) also explain the qualitative change (according to narcotism age) of the sedative PAS (hypnotics, alcohol, opiates) effect on the body, transformation of their initial sedative action into a stimulating one.

The hypertrophy of the endocrine system due to prior narcotization explains the rapid development of alcohol dependence in former opium addicts in alcoholization: rapid increase of alcohol tolerance, the rapid formation of alcohol abstinence syndrome, the developement of binge drinking (to develop alcoholism in former drug addicts, it is sufficient to develop only a specific tissue adaptation to alcohol).

Stimulation of the hypertrophic neuroendocrine system and increase in the overall resistance of the organism explain the fact that many stimulants (caffeine), eliminating some effects of ethanol, however, do not change its pharmacokinetics, prolong its intoxicating effect.

Initially the psychomotor agitation in PAS-dependent people getting narcosis can be based on the excitement of the productivity sympathetic department of VNS.

As the PAS dependence develops, functional sufficiency of VNS and the adaptation hypertrophy and hyperfunctionality of the endocrine system lead to the fact, that neuroendocrine system role as a functional mechanism of protection and adaptation increases and becomes the leading one.

II. Conclusions

1. Under regular sub-extreme exposure of the organism to psychoactive substance, physiological adaptation processes develop and lead to the hypertrophy of the endocrine system.
2. Under regular sub-extreme exposure to psychoactive substance, progredient adaptive hypertrophic changes in the endocrine system lead to an increase in the tolerance of the organism.
3. In psychoactive substances dependence, due to the adaptive hypertrophy of the endocrine system and the increased resistance, potentially extreme doses have a nonpathogenic sub-extreme effect on the organism.
4. Dependence of the body on psychoactive substances due to the increased tolerance of the organism and the transformation of the effect of potentially extreme doses into the sub-extreme effect is the adaptation process.

III. Recommendations

It is necessary to validate the dependence of the body on psychoactive substances not as a disease, but as a state of proqredient adaptation.

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Neurological Manifestations among Patients with HIV-Active Tuberculosis Co Infection

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Introduction- At least one-third of the 35.3 million people living with HIV worldwide are infected with latent tuberculosis. Tuberculosis is the most common presenting illness among people living with HIV, including those who are taking antiretroviral treatment. There were an estimated 1.1 million HIV positive new TB cases globally in 2012. Around 75% of these people live in sub-Saharan Africa. Despite its great burden, neurological manifestations have not been described yet in patients with HIV-active tuberculosis, although tuberculosis and HIV have synergistic influence on immunity system which may contribute to change in prevalence or severity of CNS involvement in patients with HIV-active TB co infection. Objectives: To study neu rological manifestations in patients with HIV-active tuberculosis.

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Neurological Manifestations among Patients with HIV – Active Tuberculosis Co Infection

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Introduction- At least one-third of the 35.3 million people living with HIV worldwide are infected with latent tuberculosis. Tuberculosis is the most common presenting illness among people living with HIV, including those who are taking antiretroviral treatment. There were an estimated 1.1 million HIV positive new TB cases globally in 2012. Around 75% of these people live in sub-Saharan Africa.

Despite its great burden, neurological manifestations have not been described yet in patients with HIV-active tuberculosis, although tuberculosis and HIV have synergistic influence on immunity system which may contribute to change in prevalence or severity of CNS involvement in patients with HIV-active TB co infection.

Objectives: To study neurological manifestations in patients with HIV-active tuberculosis

Methodology: A case series study of 58 consecutive patients with laboratory confirmed HIV- active tuberculosis co infection attending tertiary hospital for tuberculosis treatment was conducted. Data about neurological symptoms and signs – conducted by a neurologist- were collected from each patient.

Results: 24% of 58 patients were found to have neurological manifestations in clinical assessment.

Conclusion: The frequency of neurological manifestations among patients with HIV-active TB co infection was found to be higher compared to that of patients with HIV only;

I. Introduction

Sudan is the largest country in Africa, covering one eighth of the continent surface with an area of 2.5 million kms2. More than 2000 km from north to south, having diverse environment due to different climatic zones, extending from the great desert to equatorial rainy forests. Since its independence in 1956, Sudan has witnessed only eleven years of peace. The civil wars, inter-ethnic conflicts, floods, droughts and variant patterns of rain, have had adverse effects on the economic and the developmental status of the whole country. Moreover, Sudan shares extensive borders with nine countries, several of which have high HIV/AIDS prevalence. The population of Sudan according to1993 census was 26 millions. The annual growth rate also increased from 1.9 percent to 2.6 percent. Rural –urban migration has been steady and high. HIV/AIDS pandemic has become human's social and economic disaster with far reaching implications for individual communities and countries. No other disease has so dramatically highlighted the current disparities and inequities in health care access, economic opportunity, and the protection of basic human rights.

HIV belongs to the retroviruses group. AIDS was first discovered in June 1981. HIV is by far the most common immunodeficiency disorder encountered in clinical practice, it is transmitted by intercourse, heterosexual or homosexual, administration of infected blood or blood products, contaminated needles and from infected mothers to their infants. (1, 2) HIV virus causes an infection that leads to profound immune suppression. The clinical manifestations of AIDS depend on the level of immunity, which is reflected by the CD4 and T cell count. The clinical expression of HIV infection is very diverse, varying from a healthy carrier state to potentially fatal opportunistic disease. (3-4) The clinical manifestations associated with HIV infection vary in different populations, possibly due to the relative frequency of endemic infections. HIV is known to affect most of the systems including the CNS. The Neurological complications of AIDS are due either to a direct effect of the virus or to the coexistent AIDS related cancer such as lymphoma, or to opportunistic infections like toxoplasmosis. (5, 6) The neurological complications of AIDS range from acute febrile illness at the time of sero conversion to late onset dementia related to specific brain damage by the virus. HIV may cause damage to the brain causing encephalitis; it may affect the membranes surrounding the brain (meningitis). It may also cause difficulties in thinking and behavioral changes. (7,8). AIDS dementia complex is a well-recognized complication of HIV infection (9). Peripheral neuropathy, retinitis, myelopathy, demyelination and cerebral space occupying lesions, all can be seen during the course of the disease. (10)

Tuberculosis (TB) is an ancient disease. Egyptian mummified remnants dated to 3400 BC showed evidence of Pott's disease1. A recent resurgence of TB in both developing and developed countries had been observed. Several factors had

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contributed to this serious phenomenon including the increasing prevalence of HIV infection. TB of the central nervous system is a common clinical problem in developing countries. Its incidence is directly proportional to the prevalence of TB infection2. No part of central nervous system is spared. (11, 12) Infection of the meninges by tubercle bacilli is usually caused by rupture of subependyma tubercle into subarachnoid space rather than by haematogenous seeding in the meninges. The clinical manifestations of central nervous system involvement depend on the site affected. Neurological manifestations are common in patients with TB. However, high index of suspicion is needed to avoid delay in diagnosis and management. Pott's paraplegia and peripheral neuropathy were highly prevalent. (13, 14)

The paraesthesias seen in patients who presented with neurological complications- may be due to antituberculous chemotherapy, neuropathic numbness, or concomitant HIV infection17. Sphincteric disturbance in form of urine retention occurred in 10% of tuberclous patients; it is associated with Pott's paraplegia and indicates severe damage to the spinal cord. (15-16)

Cranial nerves involvement may be part of the manifestations of tuberculous meningitis especially basal meningitis, tuberculoma or may be due to coexistent diseases like HIV infection .Convulsions may be due to increase intracranial pressure in cases of tuberculoma, abscess formation, hydrocephalus complicating tuberculous meningitis, or coexistent HIV. (17, 18-19-20)

II. Objectives

To study neurological manifestations in patients with HIV-active tuberculosis.

III. Methods

The study was carried out at Bashair Teaching Hospital and Abo Anga Teaching Hospital, during the period march 2018 to May 2018. A total of 54 with HIV-active tuberculos patients were included in the study, all of whom gave their consent to participate. All were adult Sudanese patients admitted to Bashair Teaching Hospital and Abo Anga Teaching Hospital. A comprehensive history was taken with emphasis on neurological symptoms. All patients had a thorough clinical examination. The following investigations were done, when indicated: TWBC and differential, urine analysis, blood urea and electrolyte, ESR., HB% and blood picture, CSF analysis, ELISA and Weston blot., CPK, NC study, EMG, CT brain and serology for toxoplasmosis and syphilis.

IV. Results

24% of 58 patients were found to have neurological manifestations in clinical assessment.

The following table demonstrates the neurological manifestations and their frequency.

Neurological Diagnosis

	Frequency	Percent
normal	44	75.9
AIDS Dementia	3	5.2
Meningitis	2	3.4
Grand mal epilepsy	2	3.4
cerebellar ataxia	1	1.7
GBS	1	1.7
peripheral neuropathy	1	1.7
proximal weakness	1	1.7
spastic quadriplegia	1	1.7
stroke	1	1.7
transverse myelitis	1	1.7
Total	58	100.0

V. Discussion

Three of our patients presented with AIDS encephalopathy, this is the most common neurological manifestation of AIDS. Encephalopathy or what is known as AIDS dementia complex (ADC) is a brain disorder in people with AIDS characterized by cognitive impairment that manifests as severe irreparable memory loss and disorientation, thus affecting the ability to function in social or work settings. The incidence of HIV

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encephalopathy is increasing, along with the increasing incidence of AIDS. It usually develops in advanced AIDS when CD4+ lymphocyte counts fall below 200 cells/mm. It was present in 9% of the patients. The mechanism by which HIV infection leads to ADC is likely multifactorial. Theories include: (1) Cellular proteins where the widespread pathologic damage may occur via indirect cellular responses with the secretion of chemokines, proinflammatory cytokines, nitrous oxide and other neurotoxic factors; (2) Damage to neurons may occur through the actions of specific HIV proteins, including gp120, gp41, Tat, Nef, Vpr and Rev.; (3) CNS damage by humoral immune mechanisms, as evidenced by the presence of anti-CNS antibodies in AIDS patients with dementia; (4) Altered neurotransmitter release; (5) Increases in excitatory amino acids and free intracellular calcium. Disturbances of cognitive function may be the first symptoms. Early signs of HIV encephalopathy include apathy, inattention, impaired concentration forgetfulness, mood swing. Symptoms typically progress over months, but may fluctuate or remain stable. Other neurological symptoms that can be found in an encephalopathy include myoclonus (twitching of muscles or muscle groups), nystagmus (involuntary eye movements), tremor, muscle atrophy and weakness, disequilibrium (and unsteady gait), paraesthesiae (sensory disturbances), hypothalamic dysfunction, orthostatic intolerance and postural hypotension. (21, 22)

More serious neurological symptoms such as seizures can also be found in AIDS encephalopathy. Diffuse cortical atrophy is the most common finding on CT and MRI. Both can help to rule out other conditions that might be causing the symptoms. Electroencephalogram EEG reveals generalized slowing in the later stages of ADC. In spite of the fact that seizures are rare among patients with encephalopathy but a considerable number of the patients were presented with convulsion, this may be due to co existent of other abnormalities such as electrolyte disturbances.

Neurological complications, including seizures may arise from HIV itself, tuberculoma, opportunistic infections, tumors, or drugs related complications. Seizures can occur at any disease stage (Nath et al., 2000). Regarding the underlying causes of seizures, the incidence was very high among those who had CNS lymphoma. HIV-associated CNS lymphoma is a diffuse, large-cell non-Hodgkin lymphoma that usually occurs in the brain. It is a late complication of HIV infection. HIV-associated CNS lymphoma is typically of B-cell origin. Development of this opportunistic neoplasm is associated with CD4+ lymphocyte counts less than 100 cells/mm3. Non-focal, non-specific symptoms occur in more than 50% of patients; mental status changes in one third; symptoms of increased intracranial pressure (headache, nausea/ vomiting) and/or generalized seizures in 9%. Focal symptoms in 30 to 42% of cases, including weakness or numbness, partial seizures and cranial nerve palsies (visual changes, double vision, facial numbness, facial weakness, hearing loss and/or swallowing difficulties). A hypodense or hyperdense lesions that enhances in a nodular, homogeneous, or ring like pattern where observed on CT scan of the brain. Unlike what was mentioned in the literature, Patients with CNS lymphoma had secondary epilepsy while most of them had partial epilepsy ,this is due to the late presentation of the patients in addition to inappropriate management of the patients (HAART with radiation is the mainstay of treatment) (Forsyth and De Angelis, 1996.

It did appeared that all the patients had generalized epilepsy, unlike what was reported by Labar and Harden, 1997, where they found that generalized convulsions constituted 50% of seizures among patients with AIDS (Holtzman et al., 1989). The EEGs in our patients frequently show epileptiform features similar to what was reported by Harden and colleagues where they found low-amplitude slow, monotonous EEGs associated with AIDS dementia complex. Brain MRI was found to be very sensitive to support the diagnosis of brain lesions associated with AIDS, EEG, CNS, lymphoma, Toxoplasmosis and brain abscesses. (23, 24)

The study showed that tow of our patients had meningitis and brain abscess .Brain abscess is a serious, life-threatening emergency with direct consequences on morbidity, and mortality has decreased because of advances in diagnostic modalities, antibiotic regimens and early surgical interventions. The clinical course ranges from indolent to fulminant. Most symptoms are as a result of the size and location of the space-occupying lesion or lesions. The triad of fever, headache (often severe and on the side of the abscess) and focal neurologic deficit occurs in less than half of patients. The frequency of common symptoms and signs is as follows: Headache (70%), Mental status changes (may indicate cerebral edema) (65%), Focal neurologic deficits (65%), Fever (50%), Seizures (25 - 35%), Nausea and vomiting (40%), Nuchal rigidity (25%), Papilledema (25%). A suddenly worsening headache, followed by emerging signs of meningismus, is often associated with rupture of the abscess. (25, 26) The diagnosis is strongly suspected from CT or MRI brain (Offiah and Turnbull, 2006). Like non compromised individual patients with AIDS, can be present with acute or chronic meningitis and can also be present with persistent or recurrent meningeal pleocytosis with or without meningeal symptoms. Different forms of meningitis are associated with HIV infection. They may be classified according to the

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etiologic agent, as cryptococcal, tuberculous, syphilitic, or Listeria species; others are lymphomatous or aseptic. Although HIV seropositive individuals are at increased risk of certain types of meningitis, evidence suggests that they are also more likely than the general population to develop community-acquired bacterial or viral meningitides. An early form of aseptic, HIV-associated meningitis develops within days to weeks after HIV infection. It appears as a mononucleosis-like illness and is rarely associated with encephalitis. Meningitides due to cryptococcosis, coccidioidomycosis, histoplasmosis, or other fungal infection are AIDS-defining events and occur typically with very low CD4+ lymphocyte counts. An asymptomatic form is found in one third of patients. Patients present with malaise, fever, stiff neck, photophobia, and headache. Less common findings are confusion, somnolence, seizure and personality changes. Crytococcosis is the most common systemic fungal infection in AIDS and it is on the rise with the rapid spread of AIDS. Without treatment, Crytococcosis is invariably fatal. The incidence of crytococcal meningitis, formerly a relatively rare disease, has markedly increased in recent years due to the frequent occurrence of the opportunistic infection in human immunodeficiency virus positive patients, mainly in places where protease inhibitor, nucleoside reverse transcriptase and non-nucleoside reverse transcriptase drugs remains unavailable. The fungus is acquired by inhalation and causes the initial lesion in the lungs; the pulmonary stage of infection is usually a symptomatic. The fungus disseminates in debilitated patients, usually involving the meninges (Durand et al., 1993). Meningitis may be due to cryptococcus, histoplasmosis, TB or lymphoma. (27, 28) There is a well-known recognized association between brain abscess and toxoplasmosis. Toxoplasma gondii is an obligate intracellular protozoan with a worldwide distribution. Transmission occurs from the ingestion of uncooked, infected meat or from cats via a nematode vector. Toxoplasmosis is one of the most common opportunistic infections in AIDS, so cases of CNS toxoplasmosis have increased dramatically since 1981. Toxoplasmosis is responsible for over one-third of Hussein et al. 021 neurologic symptoms in AIDS patients. CNS toxoplasmosis results from infection by the intracellular parasite Toxoplasma gondii. It is usually due to reactivation of old CNS lesions or to hematogenous spread of a previously acquired infection. For most HIV-infected patients, toxoplasmic encephalitis develops after the CD4 count falls below 100. Clinical CNS toxoplasmosis occurs in 3 - 10% of patients with AIDS. Nervous system complications include encephalitis, large brain lesions in the course of AIDS and, rarely, myelitis, polyradiculoneuritis and polymyositis. In a pregnant woman, infection during the first two trimesters of pregnancy, this can result in a massive injury to the fetal encephalon, producing brain malformations, encephalopathies, psychomotor delay and chorioretinitis and epilepsy. Reported seizure rates range from 18 to 29% and may include partial, complex partial and generalized seizures. The CT scan is very suggestive as it shows multiple ring-enhancing cysts surrounded by perilesional edema. Diagnosis is supported by resolution of clinical signs and brain lesions in response to treatment. Diagnosis is more difficult when the CT scan shows a single image suggestive of abscess, or when normal. Toxoplasma serology contributes little to the diagnosis. The MRI detects multiple T2 hypersignals with mass effect. Brain biopsy, performed less often nowadays, shows areas of necrosis with parasitic infestation. A very important argument favoring the diagnosis is the effectiveness of the specific treatment, resulting in clinical and imaging resolution in over 80% of cases (Porter, 1992). (29-30).One of the rare causes of epilepsy is Progressive multifocal leukoencephalopathy (PML). Progressive multifocal leukoencephalopathy (PML) is a rare disorder that damages the material (myelin) that covers and protects nerves in the white matter of the brain, it is most common among individuals with acquired immune deficiency syndrome (AIDS). The disease occurs in 4% of adults with AIDS. Typical symptoms associated with PML are diverse, since they are related to the location and amount of damage in the brain and evolve over the course of several days to several weeks. The most prominent symptoms are Headaches, Loss of coordination, clumsiness, Loss of language ability (aphasia), Memory loss, Vision problems, Weakness of the legs and arms that gets worse, seizure and sometimes, personality changes (De Gans and Portegies, 1989).

One patients presented with neuropathy, HIV-active tuberculosis can cause peripheral nerve damage. Other causes of peripheral neuropathy include co-existent opportunistic infections, lymphoma and drugs like AZT and INH. HIV-active tuberculosis patients can present with sensory or motor neuropathy, it can cause polyneuropathy, radiculopathy and mononeuritis multiplex. Guillin-Barrie chronic inflammatory demyelinating chronic inflammatory demyelinating polyradiculoneuro pathy (CIDP). Human immunodeficiency virus (HIV) associated Guillain- Barré syndrome has been reported since 1985. This neuropathy typically occurs early in HIV infection, even at serocon version stage thus it could be the first manifestation of the infection1. It can occur at a later stage also. The pathogenesis of AIDP (acute inflammatory demyelinating polyneuropathy) is probably autoimmune, but in advanced HIV (AIDS) is usually due to CMV infection. (1-3) However, HIV associated neuropathies like distal sensory polyneuropathy and toxic neuropathies have become the most frequent

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neurological disorders in HIV infection. AIDP in HIV is not common.

Transverse myelitis can occur in AIDS with active tuberculous patients. It is a neurological disorder caused by an inflammatory process of the grey and white matter of the spinal cord, and can cause axonal demyelination. One major theory of the cause is that an immune-mediated inflammation is present as the the Result of exposure to a viral antigen. The lesions are inflammatory, and involve the spinal cord on both sides. With acute transverse myelitis. The lesions can be present anywhere in the spinal cord. Symptoms include weakness and numbness of the limbs as well as motor, sensory, and sphincter deficits. Severe back pain may occur in some patients at the onset of the disease. The symptoms and signs depend upon the level of the spinal cord involved and the extent of the involvement of the various long tracts. In some cases, there is almost total paralysis and sensory loss below the level of the lesion. If the high cervical area is involved, all four limbs may be involved and there is risk of respiratory paralysis. Lesions of the lower cervical (C2-T1) region will cause a combination of upper and lower motor neuron signs in the upper limbs, and exclusively upper motor neuron signs in the lower limbs. A lesion of the thoracic spinal cord (T1-12) will produce a spastic paraplegia. A lesion of the lower part of the spinal cord (L1-S5) produces lower motor neuron signs in the lower limb. The degree and type of sensory loss will depend upon the extent of the involvement of the various sensory tracts, but there is often a "sensory level" (at the sensory segmental level of the spinal cord below which sensation to pin or light touch is impaired). This has proven to be a reasonably reliable sign of the level of the lesion. Bladder paralysis often occurs and urinary retention is an early manifestation. (3132)

Myelopathy occurs in AIDS patiénts with active tuberculosis, it is due either to the effect of the virus, associated electrolyte disturbance or to the toxic effect of the drugs. Vaculor myelopathy typically presents as subacute progression of motor and sensory deficits over several months. Parasthesia or numbness of the limbs, if present, is sometimes is difficult to distinguish from symptoms of peripheral neuropathy, moreover, the condition often coexist in patients with advanced HIV disease. Brisk tendon reflexes suggest spinal cord or brain involvement, whereas peripheral neuropathy is associated with depressed reflexes, especially those of the Achilles tendons, a patient with both processes might have brisk knee reflexes and absent ankle jerks.

CVA is due to infarction or hemorrhage. (33, 34) HIV-active tuberculosis increases the risk of both ischemic and hemorrhagic stroke. this increased risk is most apparent in the young HIV infected population in which other risk factors for stroke are seldom evident. The increased risk include opportunistic infectious meningitides and vasculitides, primary HIV vasculopathy, altered coagulation and cardio embolic events, although the cause may be multi factorial or remain cryptic. Higher viral loads increased the risk of stroke, whereas being on antiretroviral therapy for a longer time and having an undetectable viral load decreased the risk.

Only one patient presented with cerebellar ataxia. Cerebellar complications of HIV infection primarily manifested in ataxia usually arise as the result of cerebellar lesions due to HIV encephalopathy, opportunistic infections like toxoplasmosis, vasculitis or neoplastic processes.

VI. Conclusion

HIV-active tuberculosis is a great mimicker. It can present with almost any neurological manifestation. The physician cannot be overcautious to include it in his/her differential diagnosis of otherwise unexplained neurological symptoms and signs.

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Maniology

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Abstract- The work shows the role of the autonomic Nervous system in functioning of long-term memory, the identity of functioning of the mechanisms of long-term memory in the evolutionary adaptation of a man and dependence on psychoactive substances. It is shown that the dependences of the body on psychoactive substances are the states of progredient adaptation, that the states of dependence of the organism on psychoactive substances and on psychogenic psychoactive factors are the states of the same type. Classification of psychoactive factors is given. It is proposed to create a new branch of medicine combining study of the body's dependence both on chemical and psychogenic psychoactive factors. Onomastic definitions to be used in this new branch of medicine are presented

Keywords: hypermnesia, engrams of euphoria or any other psychotropic effect, desirable from the point of view of the consumer.

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Maniology

Baitubaev D. G. [α] & Baitubaeva M. D. [σ]

Abstract- The work shows the role of the autonomic nervous system in functioning of long-term memory, the identity of functioning of the mechanisms of long-term memory in the evolutionary adaptation of a man and dependence on psychoactive substances. It is shown that the dependences of the body on psychoactive substances are the states of progredient adaptation, that the states of dependence of the organism on psychoactive substances and on psychogenic psychoactive factors are the states of the same type. Classification of psychoactive factors is given. It is proposed to create a new branch of medicine combining study of the body's dependence both on chemical and psychogenic psychoactive factors. Onomastic definitions to be used in this new branch of medicine are presented.

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I. Urgency of the Issue

Identification and increase in the number of the organism's dependencies on various external factors of psychogenic origin makes us wonder whether they have the same biological mechanism of occurrence as the body's dependence on chemical psychoactive substances. And whether these states are states of the same type?!

Purpose and objectives of the study. Hypermnesia as an integral part of the mechanism of human evolutionary adaptation. The role of the autonomic nervous system in long-term memory performance.

It is a well-known fact that in long-term memory of a person, the effects of external factors remain longer, if they caused strong emotional reactions. Emotional memory is formed very quickly and often from the first time (unlike conditional memory). This phenomenon played an important role in the survival and evolutionary development of human. Memorizing such a psychogenic factor as a predator's attack, accompanied by pavor, allowed to avoid predators in the future. Memorizing situations accompanied by positive emotions – meeting the food needs, influence of heat - contributed to seeking the influences beneficial for the body in the future.

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The leading role in the memory formation is played by the limbic system. But studying the mechanisms of long-term memory functioning reveals the instant dependence of the strength of fixation of some external influences in memory on the severity of the emotional responses accompanying those effects. This fact make us to pay attention to the role of the autonomic nervous system (ANS). Indeed, one of the main components of emotional responses are the responses of the autonomic nervous system showing as various bodily sensations: changes in the heart rhythm, increase or decrease in muscle tone, etc.

According to a hypothesis of the Canadian scientist Hebb (1949) [1], the transition of information from short-term to long-term memory occurs due to the formation and fixation of very complicated, stable structural chemical changes at the systemic, synoptic, and cellular levels. This leads to consolidation of neurons with high synaptic conductivity and formation of memory engrams fixing the external situation and the subject's attitude to it. When speaking about the regulation of synaptic efficiency, attention is paid primarily to the systems of biologically active substances serving as intermediate agents in synaptic transmission, to factors providing modulation of the efficiency of synaptic transmission and the long-term preservation of these shifts in the neural networks.

So, Kendel (1986) [1], Kruglikov (1986) [1], E. G. Gromova (1980) [1] in their studies have established that acetylcholine affects the synthesis of new receptor molecules or the unmasking and activation of already existing receptor proteins, the sensitivity of cortical neurons increasing up to recording the trace in the memory. Noradrenergic mechanisms of the brain provide the creation and temporary preservation of multineuronal constellations - engrams, the serotonergic system accelerates the learning process, facilitates fixation of engrams, and elongates the skill retention. Long-term memory processes are affected by GABA and glutamic acid. According to G. Ungar (1977) [1], I.P. Ashmarin (1987) [1], neuropeptides together with mediators, create specific receptor mosaic sets on the postsynaptic membrane that facilitates the rapid conduction of a certain type of excitation. Adrenocorticotropic hormone (ACTH) and corticosteroids, endogenous opioids - endorphins and enkephalins - have a pronounced effect on learning and memory.

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Thus, the "keeper" for all forms of neurological memory is the system of interneuronal interactions, and the participation of neurotransmitters, neuropeptides, information biopolymers consists in their influence on the quality of these interactions, their fixation. That is, the neurotransmitters released by the ANS in response to an external stimulus are a sort of modulators of transition and fixation of information in long-term memory.

Identity of the mechanisms of hypermnesia of psycho emotional effects under the influence of psychoactive substances to the evolutionary adaptive mechanism of hypermnesia.

Memory is a constantly functioning neurodynamic system. The effects of any external factor regardless its nature – psychogenic or chemical, causing positive, favorable shifts in the person's psychophysical well-being are recalled more often, and a person subconsciously seeks to re-experience the effect of this factor. Therefore, the engrams of positive emotions serve as stigma-attitudes resulting in the person's adjusting behavior. They serve as a starting point for the beginning of the psychic dependence of the body on the external factor that caused a positive psychophysical shift in a person. The repeated influence of an external psychoactive factor contributes to a greater psychic stigmatization of a person. It is noticed that during the influence of the psychoactive factor, the sensations caused by the influence of the accompanying stimuli without psychoactive properties are also fixed at the same time. This indicates that the overall hypermnesticity of the brain increases under the influence of the psychoactive factor. Therefore, engrams of the emotional memory of euphoria, are able in the future to be stimulated by the influence of concomitant stimuli too - the environment in which the psychoactive factor was active, etc.

As humanity reveals that positive (from the point of view of the consumer) emotions can be caused by the use of alcohol, opium, marijuana, tobacco, this has led not only to the increase in the habitual, regular use of these substances, but also to the awareness of the fact that it can cause dependence and affect not only the consumer of these substances, but also the society at large.

These substances were classified under the general name - psychoactive substances (abbreviated as PAS).

The development of industrial production of alcohol and the chemical industry, the increase in the number of people suffering from dependence on various psychoactive substances, considering the dependence on psychoactive substances as a disease, the need for studying and treating such dependences, all this resulted in the creation of a medical branch - narcology.

Object and methods of investigation: Vegetotropic properties of psychoactive substances. Physiology of progredient adaptation. Mechanisms of fixation of the effects of psychogenic psychoactive factors in long-term memory.

Almost all dependence-producing psychoactive substances turned out to have vegetotropic properties – primarily, they affect VNC receptors, causing the release of neurotransmitters. As it was mentioned above, neurotransmitters modulate the preservation of psycho emotional responses in long-term memory after the influence of these substances. "Catalyzing" role of neurotransmitters in long-term memory functioning can be confirmed by the fact that people with different types of dependence remember their feelings of the first episode of smoking, drinking alcohol, drugs even in decades. And it turned out that the more pleasant the subjective effect under the influence of a substance is and the more pronounced vegetative responses brightening the emotions are, the stronger the fixation of these sensations in long-term memory is and the higher the rate of occurrence of dependence is. This phenomenon is designated as narcogenicity of the substance. So, psychoactive substances with high narcogenicity – opiates – cause the accelerated development of dependence. But under the influence of substances with low narcogenicity, the occurrence of dependence requires the abuse period.

One of the urgent issues of medicine is the explanation of the biological mechanism of increasing resistance in a PAS-dependent person.

No matter how accurately scientific research explain qualitative changes at the cellular, molecular level, leading to an increase in resistance in a PAS-dependent person - these changes are obviously to have non-damaging, adaptive nature, otherwise they wouldn't lead to the increased resistance. And according to the dialectical principle of the mutual transition of qualitative changes to quantitative ones, the accumulation of these changes should lead to qualitative and quantitative changes in the system responsible for the adaptation of the body as a whole - in the neuroendocrine system. A new field in the physiology of adaptation – progredient adaptation, discovered by Baytubaev D. G. and Baytubaeva M. D. 2017 [2], based on the ability of the neuroendocrine system to hypertrophy under regular PAS exposure, allowed validating PAS-dependences not as diseases, but as states of progredient adaptation.

After all, in the 30s of the last century, P.K. Anokhin described the phenomenon of "advanced excitation", when the neuroendocrine system, in response to an external stimulus, makes an excessive release of neurotransmitters, hormones and take a pause for self-restoration, during which the assimilation-restoration processes in the endocrine system dominate

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over processes of dissimilation. The regular predominance of assimilation processes over the processes of dissimilation under the PAS exposure leads to the hypertrophy of endocrine system. Histological evidence is the Selje's stress study: "the adrenals bloom" - the adrenal medulla – the modified sympathetic ganglion [3] -which during a pause, recovers and avoids exhaustion. The adrenal cortical zone, producing hormones adaptation-corticosteroids, is hypertrophied. Also, another urgent issue of medicine is the validation of the physiological process resulting under the influence of increasing doses of a psychoactive substance and the response increase in body toleranc .

Hypertrophy of the endocrine system leads to the direct growth of the adaptive capabilities of the organism relative to the exposure dose growth, and every subsequent, potentially pathogenic, extreme dose "is met" by the hypertrophied, hyper productive endocrine system and the dose has already sub extreme - not a pathogenic - effect. That is, on each floor of adaptation, under the influence of a new increased dose of PAS, the body primarily experiences stress with orientation and resistance phases. But later the stage of depletion does not occur, since earlier due to extra output of neurotransmitters, the endocrine system "took pauses" during which assimilation processes dominated over dissimilation processes and hypertrophy of the endocrine system occured. So, the endocrine system is ready again to protect the body against the larger dose of PAS. The states of regular stress and chronic stress differs in pauses. It is conceivable that stress, whatever regular it may be, without depletion phase is not a disease. Also, while under the influence of normal pathogenic factors without vegetotropic properties first some tissue is damaged, and only after that the ANS produce a protective response, PASs, in contrast, affects primarily the receptors of the ANS, due to their vegetotrophy. This results in the timely high-level protective response of the body, preventing damage. Endocrine system hypertrophy, and therefore its high adaptive sufficiency, not only prevents damage, but also eliminates the need to compensate for the adaptive capabilities of the body at the expense of some tissues, systems of the body, so the disease does not develop. ANC productivity due to compensatory, excessive release of neurotransmitters explains adrenergic tension in deprivation syndrome, too. Productivity of the sympathetic part of the ANS against the background of the gradual exhausion of the parasympaticus (the adrenergic system is more stable in ontogenesis, too) explains - according to "the age" of narcotism - the transformation of initial sedative effect of hypnotics, alcohol and opiates into their stimulating effect. In the final stages of PAS dependence, depletion of the adaptive capabilities of the organism (the receptors of the protective systems alarm about it) leads to a concurrent decrease in the PAS doses tolerated by the dependent person, the body being not damaged repeatedly. Any pathology in PAS dependence is an associated event.

Over time it has been observed, that the dependence can occur in a person under the influence of psychogenic factors too: people who committed bad sexual crimes can develop overanxiety to repeat them, the state of falling in love results in affection and attraction to the object of love. These situations, as well as in PAS dependence, are accompanied by strong emotions and vegetative responses: fear and excitement in case of crime, a feeling on top of the world in case of love, etc. They provide fixation of the effects of these psychogenic psychoactive factors (PAFs) in long-term memory. Also, like in PAS dependence, vegetative responses under the influence of psychogenic PAFs increase the overall hypermnesticity of the brain - those who commit serial sexual crimes remember in detail every crime they commit, the lovers remember their first meeting, etc. With the development of civilization, a lot of psychogenic factors capable of causing dependence emerged. These are ideological psychogenic influences - totalitarian and authoritarian regimes, cult of personality, radical religious schools and sects, modern information technologies, and so on.

Results of the study and their discussion: Dependence on chemical and psychogenic psychoactive factors for the state of the same type.

It turned out that the dependence can be caused by exposure to any psychogenic external factor, if it resulted in the subject's strong, positive (from his/her point of view) emotions accompanied by bodily sensations. Indeed, in parties and sects with totalitarian ideology, personality cult, authoritarian regimes, under Nazism and racism - psychogenic psychoactive influences are carried out. These effects are intended to deceiving into belief about the "selectness" of the adepts, the achievement of "perfection" or the utopian "bright future," the "outstanding" abilities of the head of the state, the "selectness" of the nation, the race. These beliefs lead to positive psychosomatic shifts in the individual, group or community of people: inspiration, placidity, winged sentiment, thuggish behavior, elation, etc., inducing long-term memory to form and remember the engrams of euphoria corresponding to the influencing psychoactive factor. Psychogenic psychoactive factors also can have a narcogenic effect. Some factors can cause a psycho emotional "splash" captured by long-term memory even after a single exposure, for instance, "love at the first sight" in love mania. Meanwhile, for the dependence on psychogenic factors with low narcogenicity - totalitarian political regimes, the personality cult - a prolonged ideological

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psychoactive influence is required. The rate of dependence development varies according to the reactivity of the autonomic nervous system: emotional people are more susceptible to various kinds of mania. People with reduced psycho emotional functionality ("emotionally greedy") and with the torpid psycho emotional sphere ("emotionally phlegmatic") are less susceptible to various dependences.

All this undoubtedly indicates that the dependences on psychogenic factors are the states of the same type as the dependences on PASs. To denote the whole variety of factors of chemical and psychogenic origin capable to cause dependence, the term "psychoactive factors" is acceptable. The psychoactive factor (PAF) is a psychogenic or chemical factor that can cause euphoria or other psychotropic effects desirable from the point of view of the consumer even after single exposure, and in a regular exposure they can cause psychological-psychic or psychological-psychophysical dependence.

Differentiation of the states of progredient adaptive dependence of the body. Classification of psychoactive factors.

The principal difference between the state of progredient adaptation dependence and addiction consists in psychic stigmatization - the formation of stable neuronal engrams in the biological structures responsible for long-term memory, that affects further human behavior and creates a permanent psychic dependence on PAFs. But in addictions, processes occur at the psychological level, relatively stable conditional connections arise, and a relatively stable psychological dependence on the behavioral pattern arises – dependence on stereotypes of behavior, habits, ways of responding to some external psychogenic stimulus, etc. Although it is clear that in progredient adaptive dependences both on chemical and psychogenic PAFs, addictive behavior also takes place. Sometimes it is formed after the development of psychic dependence: when using heroin, at first a psychic dependence is formed, then the stereotype of the addict's behavior is formed. And in dependencies on chemical PASs with low narcogenicity - tobacco and alcohol - psychological addiction, such as imitative smoking, alcoholic traditions - is formed at first, and then, in abuse, psychic and further psychophysical dependences are formed.

Under the influence of psychogenic PAFs capable of exerting a mass influence, such as the cult of personality, totalitarian regimes, one part of the society may develop a psychic dependence, while the other one only develops the psychological dependence - addictive behavior.

It is necessary to differentiate the states of progredient adaptive dependence from the person's appetencies conditioned by endocrine diseases (i.e. bulimia - gluttony, polydipsia - unquenchable thirst) and psychic illnesses when emotions caused by delusional ideas dominate in the psychoemotional sphere of a mentally ill person. Clinical identification of mental dependence on a PAS in a dependent person is possible.

II. The Progression of the Hypermnesia Processes

Feelings of positive psychophysical shifts under the influence of the PAF are fixed in memory. Such fixation is enhanced due to the regularity of PAF influence and the quantitative increase in the force of influence. That explains the stability of dependence on drug addiction, totalitarian political and religious ideologies, etc. The expansion of the memory engrams about positive psychophysical shifts is due to the memorization of concomitant stimuli accompanying the PAF influence. That explains the existence of rituals of joint smoking, alcohol consumption. All the mentioned above indicates the formation of adaptive, super-strong, expanded memory hyperengrams.

In PAF dependence changes in the biological mechanisms responsible for the euphoria hypermnesia are of a physiological, adaptive nature, and the available types of treatment consist only in blockade of the adaptation mechanisms against the repeated PAF influence. In this regard, euphoria hyperengrams remain saved in long-term memory and generally are the only cause of relapse. That is why a person dependent on illegal sexual activity can commit a sexual crime after having served long prison terms. Alcohol or drug dependent people after successful treatment and prolonged remission can resume alcohol and drug use. For love mania there is the expression "to fell in love for a lifetime". Dependences on psychogenic PAFs (the cult of personality, totalitarian ideologies) persist up to the alternation of generation. The following studies are considered to be promising: studies of neurophysiological mechanisms of formation and fixation of euphoria engrams or other psychotropic effects desirable from the point of view of the consumer in the memory, development of methods of selective neutralization-"erasure from memory" of euphoria engrams (by patient's consent).

III. Classification of Psychoactive Factors

1) Psychogenic PAFs:

a) Psychogenic PAFs capable of causing a mass adaptive psychological and psichic dependence: totalitarian and authoritarian political ideologies, the ideology of racism, Nazism, the cult of personality.

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b) Psychogenic PAF capable of causing a group adaptation psychological and mental dependence - of religious and other totalitarian sects.
c) Psychogenic PAF - illegal actions capable of causing individual adaptation psychological and psychic dependence - dependence on sexual acts, prohibited by law, kleptomania, pyromania, etc. (all the above-mentioned PAFs are prohibited or should be prohibited by law).
d) Other psychogenic PAFs (influences) capable of inducing an individual progredient adaptational psychological and psychic dependence - a state of falling in love, game addiction, etc.

2) Chemical PAFs:
a) Chemical PAFs with high narcogenicity capable of inducing the accelerated development of individual progredient psychological and psychophysical adaptation dependence - drugs. (non-medical use and illegal trafficking are prohibited by law).
b) Chemical PAFs capable of inducing an individual progredient psychological and psychophysical adaptation dependence in case of abuse - alcohol, tobacco, etc.

Should other psychogenic and chemical PAFs dangerous to the individual and society are identified, they must be listed as prohibited by law.

IV. Maniology

Narcology can only be a section of a new, broader branch of medicine that studies dependences both on chemical and psychogenic psychoactive factors. To denote a new branch, the term "maniology" is acceptable. (mania-propensity, appetency, Logos doctrine, i.e, the doctrine of propensities, appetencies).

Maniology is a branch of medical science that studies adapto genesis and adaptive manifestations of the progredient adaptation psychic-psychological and psychological-psychophysical dependence of an individual, a group of people and a society on various chemical and psychogenic psychoactive factors of the environment, medical, psychological, social and legal aspects of these problems, and develops methods of their prevention, treatment of deprivation syndrome and neutralization of appetency for the psychoactive factor.

In this regard, some definitions of various maniology sections, for example, narcology, should be changed.

Narcology is a section of maniology as a medical branch, which studies the adaptogenesis and adaptive manifestations of a person's progredient adaptation psychological-psychophysical dependence on various chemical psychoactive factors, the medical, psychological, social and legal aspects of these problems, and develops methods for their prevention, treatment of deprivation syndrome and neutralization of appetency for chemical psychoactive factor.

To develop a new branch of medicine, there is a need in formation of Maniology scientific departments in higher medical schools.

V. Conclusions

1. Hypermnesia of external influences accompanied by strong emotional responses is an integral part of the evolutionary adaptive mechanism of the body.
2. The neurotransmitters released by the ANS in response to an external stimulus causing strong emotional responses are modulators of transmitting information from short-term to long-term memory.
3. The mechanism of preservation of psycho emotional sensations in long-term memory under the influence of psychoactive substances is identical to the evolutionary adaptive mechanism of hypermnesia.
4. Dependences of the body on psychoactive substances are the states of progredient adaptation.
5. Identity of the mechanisms of fixation of psycho emotional sensations in long-term memory under the influence of chemical and psychogenic psychoactive factors allows us to suggest that these states are states of the same type.
6. The presence of a psychic component in the appetency for any PAF is a distinctive feature of the state of adaptive progredient dependence on PAF, on the state of behavioral addiction and other appetencies.

VI. Recommendations

It is necessary to create a new branch of medicine combining the study of human dependence both on chemical and psychogenic psychoactive factors.

Hypermnesia of euphoria or any other desired, from the point of view of the consumer, psychotropic effect as the initial and leading link in the occurrence and maintaining the body's dependence on psychoactive factors

The work shows the role of the autonomic nervous system in functioning of long-term memory, the identity of functioning of the mechanisms of long-term memory in the evolutionary adaptation of a man and dependence on psychoactive substances. It is shown that the dependences of the body on psychoactive substances are the states of progredient adaptation, that the states of dependence of the body on psychoactive substances and on psychogenic psychoactive factors are the states of the same type. It is proposed to create a new branch of medicine combining study of the body's dependence both on chemical and psychogenic psychoactive factors.

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Classification of psychoactive factors is given. Onomastic definitions of terminology changes and additions to be used in this new branch of medicine are presented. Proposed allocation of the International Classification of Diseases is a separate chapter for the classification of states of progredient adaptation of the body depending on psychoactive factors.

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Evoked Brain Potentials in the Preoperative Diagnosis of Type 1 Chiari Malformation

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Abstract- The scientific work presents the results of neurophysiological examination of 207 patients with Chiari malformation of type 1 according to MRI data. All patients underwent a multimodal protocol, including acoustic stem evoked potentials, somatosensory evoked potentials, and electroneuromyography. The diagnostic criteria for neurological syndromes - cerebellar, bulbar, pyramidal, syringomyelitis in Chiari malformation of type 1 according to neurophysiological data - were identified. A clinical and neurophysiological point scale for the choice of conservative or surgical tactics has been proposed.

Keywords: chiari malformation 1, acoustic brainstem evoked potentials, somatosensory evoked potentials, electroneuromyography

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Keywords: chiari malformation 1, acoustic brainstem evoked potentials, somatosensory evoked potentials, electroneuromyography.

I. Introduction

The rapid development of computer technology predetermined a new stage in the formation of clinical neurophysiology. Improvement of the system equipment makes it possible to adequately assess various functional parameters of cerebral and spinal structures, to conduct their dynamic observation (6, 8, 14).

Evoked brain potentials - acoustic stem evoked potentials and somatosensory evoked potentials have the greatest diagnostic value in determining the functional state of the brain stem structures and spinal conducting systems (10, 12, 13). In modern publications, there is no consensus on the neurophysiological aspects of clinical syndromes of Chiari malformation 1 - cerebellar, bulbar, pyramidal, syringomyelitis (2, 4, 5, 7). Also, we did not find definite data on the choice of treatment tactics for Chiari malformation of type 1 caused by neurophysiological changes. Currently, neurologists and neurosurgeons, when choosing a therapy for patients with Chiari malformation of type 1, rely mainly on the data of subjective complaints, neurological examination and the degree of tonsil ectopia by MRI (1,3,9,11). However, this whole complex does not fully give an objective picture of the functional state of the stem structures, especially in case of subclinical forms of pathology. This circumstance was the reason for us to conduct clinical and neurophysiological comparisons of the indicated syndromes with type 1 Chiari malformation and the development of neurophysiological characteristics of various clinical syndromes of Chiari 1 malformation according to the data of acoustic stem, somatosensory and motor evoked potentials.

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II. Materials and Methods

Examined 207 patients with Chiari malformation 1 according to MRI studies, who are on outpatient and inpatient treatment at the Republican Specialized Scientific and Practical Medical Center of Neurosurgery, Ministry of Health of the Republic of Uzbekistan. The standard in determining the degree of omission of the cerebellar amygdala in Chiari malformations was the Chamberlain line, which runs from the hard palate to Opistion (2,8,9). We considered the displacement of the cerebellar tonsils beyond the Chamberlain line up to 5 mm admissible. In our studies, we used exactly the Chamberlain line to guide the anatomical anomalies of the craniovertebral junction and the degree of ectopia of the cerebellar tonsils (Fig. 1, 2).

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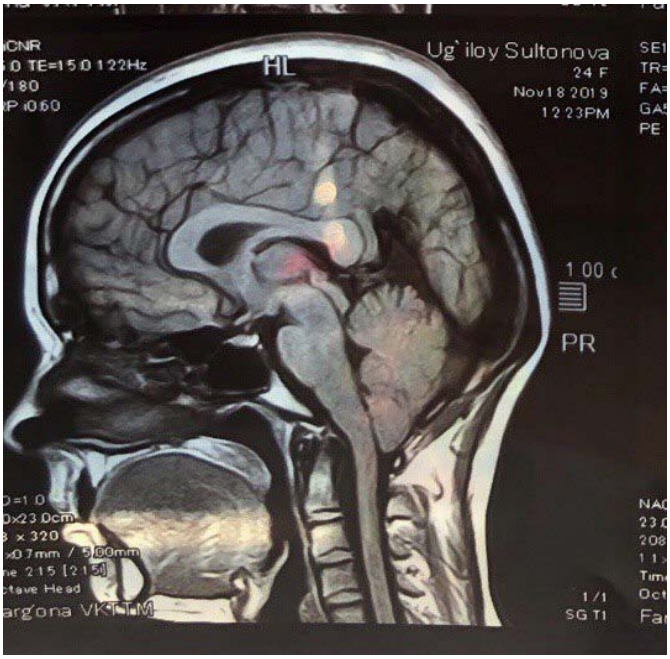


Figure 1: An example of MRI of patient S., with Chiari malformation of type 1 with ectopia of cerebellar tonsils 14mm on the right and 12mm on the left

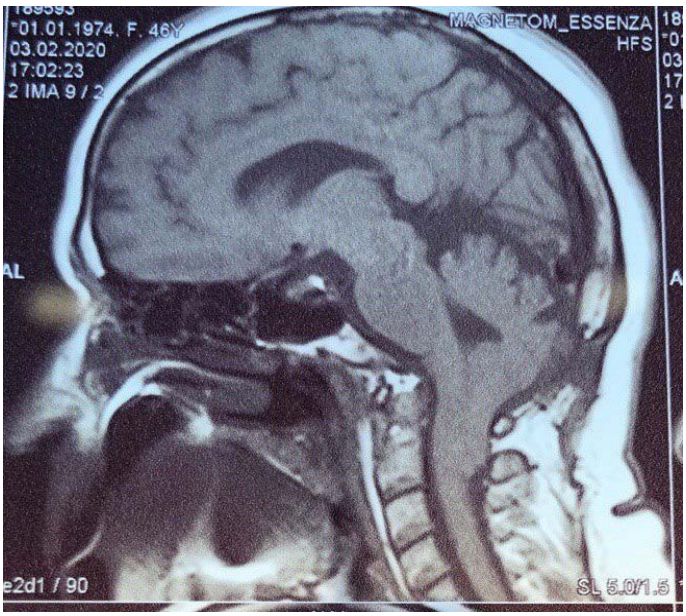


Figure 2: MRI of patient Z., 34 years old, with an anomaly of the craniovertebral junction with displacement of the cerebellar tonsils below the Chamberlain line up to 24 mm from 2 sides

We analyzed clinical symptoms in 207 patients with Chiari malformation of type 1 according to MRI data. Of these, 73 are men and 134 are women between the ages of 14 and 62. In the structure of neurological syndromes, 82 patients with cerebellar syndrome, 26 patients with manifestations of bulbar syndrome, 21 patients with pyramidal syndrome and 78 patients with clinical symptoms of syringomyelitis syndrome were examined.

All patients were examined according to a multimodal neurophysiological protocol, including acoustic stem evoked potentials, somatosensory evoked potentials, and motor evoked potentials (7). The studies were carried out on a 4-channel "Synapsis" complex (Neurotech, Russia) with computer data processing.

For the included acoustic stem evoked potentials, a standard vertex-mastoidal lead (M1-Cz,

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M2-Cz) was used; stimulation was performed through headphones with acoustic clicks of 0.1 ms duration biurally with a feed frequency of 20 Hz and a sound of 70 dB.

When carrying out somatosensory evoked potentials, the discharge electrodes were installed according to the standard technique (see Chapter 2) C4-Fz - with n. medianus S stimulation C3-Fz- with n. medianus D stimulation. Stimulation was carried out with electric impulses in the projection of the median nerve at the level of the wrist by current 15-20 m A, frequency 2 Hz.

We performed stimulation EMG by default for n.glossopharyngeus et n.accessorius with the setting of recording electrodes in accordance with the muscle innervation. If necessary, we supplemented the studied nerves based on the clinical syndrome.

III. Results and Discussion

a) Cerebellar syndrome in patients with Chiari malformation type 1

We studied the data of acoustic stem evoked potentials, somatosensory evoked potentials and motor evoked potentials in 82 patients - 52 women and 30 men with clinical manifestations of cerebellar syndrome and Chiari 1 anomaly. The control group consisted of 30 healthy individuals.

The obtained data, including acoustic brainstem evoked potentials - studies in patients with cerebellar syndrome are presented in Table 1. It was revealed that in all examined patients the latent periods of and peaks were extended bilaterally with significant differences compared to healthy individuals. The mean values of the latencies of the remaining components - I. II, IV, were unchanged compared with the results of the control group. The amplitude indices of the and peaks were significantly increased relative to the control values, which dissociated with the general ideas about the depression of amplitude indices with the inclusion of acoustic stem evoked potentials in patients with pathology of stem structures. In our opinion, an increase in the amplitudes of the III components in patients with cerebellar syndrome indicated functional irritation of the stem structures at the level of the superior olivary complex. Analysis of the mean values of the peak-to-peak intervals showed an insignificant delay in III, IV and I-in the study group with significant differences from the control individuals, which indicated a slowdown in conduction at the pontomesencephalic level. Peak intervals I- were preserved in comparison with the control group, which can be explained by the intactness of the peripheral portion of the auditory analyzer.

Table 1: Indicators of acoustic stem evoked potentials - latency period, peak amplitudes and inter-peak intervals in healthy individuals of the control group (n=30) and patients with cerebellar syndrome Chiari malformation 1 (n= 82)

Latent period, ms

Control group (n=30)	PI	PII	PIII	PIV	PV
S	1.79± 0.16	2.95 ± 0.18	3.94 ± 0.24	5.06 ± 0.22	5.97 ±0.25
D	1.72 ± 0.17	2.98 ± 0.19	3.92 ± 0.22	5.13 ± 0.20	6.02± 0.25
Cerebellar Syndrome (n=82)					
S	1.74 ± 0.18	2.96 ± 0.17	4.25 ± 0.25	5.25± 0.21	6.55± 0.22*
D	1.68 ± 0.16	3.02 ± 0.19	4.25 ± 0.21*	5.38± 0.19	6.70 ±0.24*

Amplitude, μV

Control group(n=30)	PI	PIII	PV
S	0.286± 0.05	0.262± 0.04	0.368 ±0.06
D	0.282± 0.04	0.265± 0.06	0.338± 0.08
Cerebellar Syndrome (n=82)			
S	0.348± 0.03	0.370± 0.03**	0.375 ± 0.05*
D	0.340± 0.04	0.372± 0.05**	0.380 ± 0.07*

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Peak intervals, ms

Control group (n=30)	PI-PIII	PIII-PV	PI-PV
S	2.19± 0.16	2.06± 0.18	4.38± 0.22
D	2.24± 0.18	2.08± 0.22	4.46± 0.24
Cerebellar Syndrome (n=82)			
S	2.56± 0.15	2.52± 0.14**	4.90±0.21*
D	2.88± 0.17	2.60± 0.18**	4.82±0.20*

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

We analyzed the data of somatosensory evoked potentials in 82 patients with clinical manifestations of cerebellar syndrome and Chiari 1 anomaly. Registration of somatosensory evoked potentials was carried out with stimulation of the median and tibial nerves from 2 sides, the average values of somatosensory evoked potentials were compared with the values in the control group. The results of the somatosensory evoked potentials of the study in cerebellar syndrome are presented in Table 2.

Table 2: Indices of somatosensory evoked potentials upon stimulation of the median nerve - latency period, peak amplitudes and inter-peak intervals in healthy controls (n=30) and patients with cerebellar Chiari malformation 1 (n=82)

Latency, ms	Controlgroup(n=30)	Cerebellarsyndrome(n = 82)
N9 Erba	9.6±0.7	9.4±0.7
N13 neck	13.2±0.8	14.5±0.7*
N20 cortex	18.8±1.0	18.9±1.2
Amplitude,μV		
N9 Erba	5.4±2.5	5.6±2.2
N13 neck	2.9±1.3	2.7±1.2
N20 cortex	2.8±1.6	2.9±1.5
Peakintervals, ms		
N9-N13	3.5±0.4	3.2±0.3
N13-N20	5.8±0.5	6.9±0.2*
N9-N20	9.2±0.5	8.8±0.7

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

As can be seen from the above proposed data, in the group of patients with cerebellar syndrome, there was a significantly significant increase in the latency of the N13 component to 14.5 ms compared to the control group, which was more often symmetric bilateral (84% of observations). The amplitude indices of all components of the somatosensory evoked potentials were preserved relative to healthy individuals. The extension of the peak-to-peak intervals N13-N20 to 6.9 ms was isolated in the group of patients with Chiari malformation 1; the parameters of the peak-to-peak intervals N9-N13 and N9-N20 were unchanged compared to the control values.

When analyzing these indicators somatosensory evoked potentials for stimulation of the tibial nerve, shown in Table 3, a significant extension of the latent period of the N30 component to 38.1 ms was determined in patients with cerebellar syndrome relative to the control group. Changes in the amplitudes of the components N22, N30, P37 in the studied group of patients were not recorded. The N30-P37 peak-to-peak interval was moderately extended to 12.5 ms in most cases (68%) with cerebellar syndrome compared with healthy individuals; the N22-N30, N22-P37 peak latencies corresponded to the control group.

Table 3: Indices of somatosensory evoked potentials during stimulation of the tibial nerve - latent period, peak amplitudes and inter-peak intervals in healthy controls (n=30) and patients with cerebellar Chiari malformation 1 (n= 82)

Latency, ms	Controlgroup(n=30)	Cerebellarsyndrome (n = 82)
N 22 lumbar	23.6±1.9	23.2±1.6
N 30 cervical	30.6±2.5	38.1±1.2**
P37 cortex	37.5±3.4	36.±3.0
Amplitude, μV		
N 22 lumbar	1.3±0.5	1.7±0.3*
N 30 cervical	0.9±0.3	1.1±0.2
P37 cortex	2.6±1.5	2.9±1.5

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Peakintervals, ms		
N22-N30	7.62±1.14	7.86±1.07
N30-P37	8.05±1.32	12.5±1.54*
N22-P37	15.7±1.65	16.9±1.35

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

Thus, the analysis of the data somatosensory evoked potentials upon stimulation of the median and tibial nerves revealed an increase in the latency of the N13, N30 components in patients with cerebellar Chiari malformation syndrome 1 in a predominant number of cases was combined with an expansion of the inter-peak intervals N13-N20 (64% of patients) and N30-P37 (55% of patients), which indicated a slowdown in afferentation at the level of the cervical spinal cord and then the medulla oblongata - thalamus cortex with a tendency to decrease the postsynaptic activation of the medulla oblongata nuclei.

We analyzed the electroneuromyography of the data obtained during stimulation of the oculomotor, facial, glossopharyngeal nerves, as well as the median and tibial nerves in the group of patients with cerebellar disorders and Chiari 1 anomaly. As follows from Table 4 below, the values of the speed of motor conduction of the SPI eff were insignificant. decreased in the facial and glossopharyngeal nerves with significant differences from the control group. The efferent velocity along the oculomotor nerve in the study group was preserved relative to the control. Indicators of the speed of conduction of the impulse SPI eff along the nerves of the upper and lower extremities were unchanged in comparison with healthy individuals. Also, we did not register significant deviations in the A max of the M-response amplitudes for all studied nerves in the group of patients. However, after stimulation, pathological waves along the facial nerve were observed in 27% of patients with cerebellar syndrome, whereas in the group of healthy individuals, such a phenomenon was not recorded.

Table 4: Electroneuromyography indices of oculomotor, facial, glossopharyngeal, median and tibial nerves in healthy controls (n = 30) and patients with cerebellar Chiari malformation syndrome 1 (n = 82)

Control group(n=30)	SPI, m / s	Amax, μV	Additionalpathologicalwaves
Oculomotornerve	29.4±2.2	1080±105.5	-
Facialnerve	39.5±1.8	1235±126.3	-
Glossopharyngealnerve	42.6±2.0	1860±164.0	-
Mediannerve	61.0±1.7	6254±267.0	-
Tibialnerve	49.6±2.1	7125±745.5	-
Cerebellarsyndrome (n = 82)			
Oculomotornerve	29.1±2.0	1072±105.8	
Facialnerve	34.8±1.6**	1130±138.0*	+
Glossopharyngealnerve	39.2±1.4**	1851±170.5	
Mediannerve	60.4±1.5	6158±245.6	
Tibialnerve	48.3±1.9	7245±760.8	

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

In our opinion, small deviations of the SPI eff indices towards a decrease in the facial and glossopharyngeal nerves against the background of relatively unchanged values of the M-response amplitudes testified to the functional involvement of the structures of the pons pons and medulla oblongata in cerebellar syndrome. Pathological waves along the facial nerve may correspond to irritative disorders at the cerebellopontine level. Unchanged parameters of SPI eff and amplitudes of muscle responses during stimulation of the median and tibial nerves in the group of patients with Chiari 1 malformation indicated the absence of dysfunctions of the segmental apparatus in cerebellar disorders.

b) Bulbar syndrome in patients with Chiari malformation type 1

We analyzed the neurophysiological data of 26 patients with clinical manifestations of bulbar syndrome with Chiari malformation 1 at the age of 18 to 65 years, the number of men was 9 cases, women - 17 cases. The control group consisted of 30 healthy individuals.

All patients of this group underwent an analysis including acoustic stem evoked potentials of the data, which revealed significant differences with the control group in terms of the latency parameters and amplitudes of the components presented in Table 4.5. Thus, the latency of the PIII and PV components was

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moderately extended from 2 sides compared to the control group. There was a reduction in the amplitude values of the peaks PV and PV, often bilaterally, while the asymmetry of changes including acoustic brainstem evoked potentials-indicators was recorded in 76% of the examined patients, the complete absence of PIII and PV components was noted in 24% of cases in comparison with healthy individuals. Noteworthy is the significant expansion of the peak-to-peak intervals PIII-PV and PI-PV by almost two times in the group of patients with bulbar manifestations compared to the control. In 24% of patients, it was impossible to analyze the peak-to-peak intervals due to the absence of the formation of PIII and PV components. Thus, the analysis of the above changes in the parameters of acoustic brainstem evoked potentials objectively indicated gross conduction disturbances in the clinical manifestations of bulbar syndrome in patients with Chiari 1 malformation at the level of the inferior bridge and midbrain, often asymmetrically with dissociated functional involvement of pontomesencephalic structures.

Table 5: Indicators of acoustic stem evoked potentials - latency period, peak amplitudes and inter-peak intervals in healthy individuals of the control group (n = 30) and patients with bulbar Chiari malformation syndrome 1 (n = 26)

Latent period, ms

Control group (n=30)	PI	PII	PIII	PIV	PV
S	1.79± 0.16	2.95 ± 0.18	3.94 ± 0.24	5.06 ± 0.22	5.97 ±0.25
D	1.72 ± 0.17	2.98 ± 0.19	3.92 ± 0.22	5.13 ± 0.20	6.02± 0.25
Bulbar syndrome (n=26)					
S	1.80 ± 0.18	2.98 ± 0.17	4.35 ± 0.25	5.30± 0.21	7.05± 0.22**
D	1.76± 0.16	3.01 ± 0.20	4.70 ± 0.21**	5.65± 0.19	8.01 ±0.24**

Amplitude, μV

Control group (n=30)	PI	PIII	PV
S	0.286± 0.05	0.262± 0.04	0.368 ±0.06
D	0.282± 0.04	0.265± 0.06	0.338± 0.08
Bulbar syndrome (n=26)			
S	0.348± 0.03	0.050± 0.01**	0.050 ±0.02**
D	0.340± 0.04	0.180± 0.02*	0.220± 0.04*

Peakintervals, ms

Controlgroup (n = 30)	PI-PIII	PIII-PV	PI-PV
S	2.19± 0.16	2.06± 0.18	4.38± 0.22
D	2.24± 0.18	2.08± 0.22	4.46± 0.24
Bulbar syndrome (n=26)			
S	2.36± 0.15	3.96± 0.15**	6.05±0.20*
D	2.48± 0.17	3.65± 0.20**	6.35±0.21**

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - $P< 0.05$, ** - $P < 0.01$*

We analyzed the data of somatosensory evoked potentials in 26 patients with clinical manifestations of bulbar syndrome, Chiari 1 anomaly. Registration of somatosensory evoked potentials was carried out with stimulation of the median and tibial nerves from 2 sides, the mean values of somatosensory evoked potentials were compared with the values in the control group. The results of somatosensory evoked potentials of the study in bulbar syndrome are presented in table 6.

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Table 6: Indices of somatosensory evoked potentials during median nerve stimulation - latency period, peak amplitudes and inter-peak intervals in healthy controls (n = 30) and patients with bulbar Chiari malformation syndrome 1 (n = 26)

Latency, ms	Controlgroup (n = 30)	Bulbarsyndrome (n = 26)
N9 Erba	9.6±0.7	10.1±0.8
N13 neck	13.2±0.8	18.4±1.2*
N20 cortex	18.8±1.0	18.7±1.5
Amplitude,μV		
N9 Erba	5.4±2.5	5.1±2.0
N13 neck	2.9±1.3	1.1±0.5**
N20 cortex	2.8±1.6	1.2±0.4**
Peakintervals, ms		
N9-N13	3.5±0.4	3.9±0.5
N13-N20	5.8±0.5	8.0±0.7**
N9-N20	9.2±0.5	9.8±0.6*

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

As can be seen from the above proposed data, in the group of patients with bulbar syndrome, there was a significant increase in the latencies of the N13 components up to 18.4 ms in comparison with the control group. Also, in the group of these patients, a statistically significant decrease in the amplitudes of the N13 and N20 components was recorded, often bilateral with an asymmetry in 61% of observations relative to healthy individuals. The values of the N13-N20 peak-to-peak intervals were significantly increased in the majority of patients in this group up to 8.0 ms, however, the parameters of the N9-N13, N9-N20 intervals were slightly changed relative to normal values.

Further, we studied the data of somatosensory evoked potentials obtained on stimulation of the tibial nerve in patients with bulbar syndrome with Chiari malformation 1, presented in Table 7.

Table 7: Indices of somatosensory evoked potentials during stimulation of the tibial nerve - latency period, peak amplitudes and inter-peak intervals in healthy controls (n = 30) and patients with bulbar Chiari malformation syndrome 1 (n = 26)

Latency, ms	Controlgroup(n = 30)	Bulbarsyndrome(n = 26)
N 22 lumbar	23.6±1.9	23.9±1.6
N 30 cervical	30.6±2.5	42.8±1.26**
P37 cortex	37.5±3.4	38.4±3.0
Amplitude,μV		
N 22 lumbar	1.3±0.5	1.65±0.3*
N 30 cervical	0.9±0.3	0.28±0.1**
P37 cortex	2.6±1.5	2.85±1.6
Peakintervals, ms		
N22-N30	7.62±1.14	7.80±1.05
N30-P37	8.05±1.32	17.8±1.52**
N22-P37	15.7±1.65	17.0±1.25

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

We found a statistically significant isolated extension of the N30 component latency to 42.8 ms in the group of patients with bulbar syndrome compared to the control group, while the latencies of the N22 and P37 components were relatively preserved. Also, these patients showed a reduction in the amplitude of the N30 component to 0.28 μV against the background of unchanged values of the amplitudes of the N22 and P37 components in comparison with normal values. A significant expansion of the N30-P37 peak-to-peak intervals up to 17.8 ms was recorded in the group of patients with bulbar syndrome, often had a pronounced asymmetric character (in 61% of cases) compared with the control group, although the N22-N30 and N22-P37 peak-to-peak intervals had slight deviations from the norm ...

So, the analysis of changes in the parameters of somatosensory evoked potentials for the stimulation of the median and tibial nerves in patients with clinical manifestations of bulbar syndrome indicated a pronounced slowdown in conduction at the presynaptic level of the medulla oblongata nuclei with a decrease in their activation. A pronounced retardation of afferent conduction at the pontomedullary level in bulbar disorders was combined with moderate disturbances in thalamo-cortical conduction.

Characteristics of electroneuromyo graphy - data for bulbar syndrome with Chiari 1 anomaly was

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analyzed in 26 patients. The results of the motor evoked potentials obtained by stimulation of the oculomotor, facial, glossopharyngeal nerves, as well as the median and tibial nerves are presented in Table 8.

Table 8: Electroneuromyography indices for the oculomotor, facial, glossopharyngeal, median and tibial nerves in healthy controls (n = 30) and patients with bulbar Chiari malformation syndrome 1 (n = 26)

Control group (n = 30)	SPI m / s	Amax, μV	Additional pathological waves
Oculomotor nerve	29.4±2.2	1080±105.5	-
Facial nerve	39.5±1.8	1235±126.3	-
Glossopharyngealnerve	42.6±2.0	1860±164.0	-
Mediannerve	61.0±1.7	6254±267.0	-
Tibialnerve	49.6±2.1	7125±745.5	-
Bulbar syndrome (n = 26)			
Oculomotor nerve	28.5±2.0	1072±124.8	
Facial nerve	34.1±1.6*	1180±122.0*	+
Glossopharyngeal nerve	20.8±2.6**	788±182.0**	+++
Mediannerve	54.5±1.8*	5011±256.5	
Tibialnerve	42.7±1.7	6450±628.5	

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - $P< 0.05$, ** - $P < 0.01$*

When analyzing the obtained indicators, a significantly significant decrease in the speed of the efferent impulse was revealed during stimulation of the glossopharyngeal nerve in the group of patients with bulbar syndrome in a relatively healthy group, while in 60% of the examined the parameters of SPIEff were reduced by more than 2 times compared with the control. It should be noted that even with mild bulbar symptoms, the efferent STI indices significantly differed from normal in the direction of decrease, which, possibly, reflected subclinical functional disorders. The rate of efferent conduction along the facial nerve decreased by less than 25%, and along the oculomotor nerve was relatively unchanged from the initial parameters. Along with changes in speed indicators, there was a significant decrease in the amplitudes of the M-response along the glossopharyngeal nerve, more than 2 times relative to the indicators of healthy individuals. Amplitude values of the M-response of the facial and oculomotor nerves with a tendency to decrease in the group of patients compared with the control group. Attention is drawn to the presence of pathological waves of fibrillation in 30% of patients with stimulation of the glossopharyngeal nerve, which indicated the involvement of the medulla oblongata nuclei in the pathological process. When analyzing the electroneuromyography of the data obtained during the stimulation of the median and tibial nerves, a tendency towards a decrease in the rate of conduction of the efferent impulse was recorded in the group of patients compared with healthy individuals. At the same time, the indicators of the maximum amplitude of the M-response of the median and tibial nerves were practically unchanged in comparison with the control group. This phenomenon, in our opinion, is associated with reactive involvement of the efferent pathways in patients with bulbar syndrome with the development of bilateral pyramidal insufficiency.

Thus, in the study of electroneuromyography, the bulbar syndrome was characterized by a pronounced conduction disorder at the level of the medulla oblongata nuclei, often with the capture of the intersection of the pyramidal tract. electroneuromyography data made it possible to objectively assess the condition of patients with bulbar syndrome Chiari malformation 1, even in the subclinical phase of the disease.

c) Pyramidal syndrome in patients with Chiari malformation type 1

We studied the neurophysiological characteristics of the pyramidal syndrome in 21 patients with Chiari malformation 1, including 13 women and 8 men aged 16 to 45 years. Acoustic stem evoked potentials were performed in all patients of this group. The data obtained by us in comparison with the control group are presented in table 9.

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Table 9: Indicators of acoustic stem evoked potentials - latency period, peak amplitudes and inter-peak intervals in healthy individuals of the control group (n = 30) and patients with pyramidal syndrome Chiari malformation 1 (n=21)

Latent period, ms

Control group (n = 30)	PI	PII	PIII	PIV	PV
S	1.79± 0.16	2.95 ± 0.18	3.94 ± 0.24	5.06 ± 0.22	5.97 ±0.25
D	1.72 ± 0.17	2.98 ± 0.19	3.92 ± 0.22	5.13 ± 0.20	6.02± 0.25
Pyramidalsyndrome (n =21)					
S	1.80 ± 0.16	2.90 ± 0.17	4.41 ± 0.25**	5.25± 0.21	6.55±0.22*
D	1.82 ± 0.16	2.86 ± 0.15	4.48 ± 0.21**	5.38± 0.19	6.52±0.24*

Amplitude, μV

Control group (n = 30)	PI	PIII	PV
S	0.286± 0.05	0.262± 0.04	0.368 ±0.06
D	0.282± 0.04	0.265± 0.06	0.338± 0.08
Pyramidal syndrome (n=21)			
S	0.290±0.05	0.375± 0.03*	0.380 ± 0.05*
D	0.284±0.04	0.360± 0.05*	0.385 ± 0.04*

Peak intervals, ms

Control group (n = 30)	PI-PIII	PIII-PV	PI-PV
S	2.19± 0.16	2.06± 0.18	4.38± 0.22
D	2.24± 0.18	2.08± 0.22	4.46± 0.24
Pyramidalsyndrome (n=21)			
S	2.32± 0.14	3.48± 0.14**	4.75±0.20*
D	2.29± 0.12	3.52± 0.16**	4.84±0.18*

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

As can be seen from the above proposed table, when the study included acoustic stem evoked potentials in patients with pyramidal syndrome Chiari 1 malformation, the most variable were the latencies of components and inter-peak latencies. Thus, in the group of patients, there was an increase in the latency of the P and PV peaks, often symmetric in 85% of cases, relative to the control values. The latencies of the components PI, PII, PIV were unchanged in comparison with normal values. Attention is drawn to the phenomenon of an increase in the amplitude indices of the peaks PIII and PV from 2 sides in the group of patients with pyramidal syndrome with Chiari malformation 1 relative to the control group, which, in our opinion, is caused by irritative disorders of the motor tract against the background of concomitant hypertensive-hydrocephalic symptoms. Typical disorders involving the acoustic brainstem evoked potentials of the pyramidal syndrome indicators were manifested in the protraction and expansion of the inter-peak intervals PIII-PV and PI-PV, which was significantly different in comparison with the group of healthy individuals. Moreover, in more than 80% of cases, these changes were bilateral. Thus, with the inclusion of acoustic stem evoked potentials in patients with clinical manifestations of pyramidal syndrome, a widespread deceleration of conduction at the pontomedullary level is recorded, which has a bilateral nature. The phenomena of irritation of the motor pathways can also correspond to the symptoms of pyramidal insufficiency, which in most cases developed against the background of hypertensive-hydrocephalic syndrome.

Next, we analyzed the indicators of somatosensory evoked potentials in patients with clinical manifestations of pyramidal syndrome and Chiari 1 anomaly. The resulting changes in the indicators of somatosensory evoked potentials during stimulation of the median nerve are presented in Table 10.

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Table 10: Indices of somatosensory evoked potentials during median nerve stimulation - latency period, peak amplitudes and inter-peak intervals in healthy controls (n = 30) and patients with pyramidal syndrome Chiari malformation 1 (n = 21)

Latency, ms	Controlgroup (n = 30)	Pyramidalsyndrome (n = 21)
N9 Erba	9.6±0.7	9.2±0.7
N13 neck	13.2±0.8	14.1±0.6*
N20 cortex	18.8±1.0	20.2±0.8*
Amplitude,μV		
N9 Erba	5.4±2.5	5.6±2.0
N13 neck	2.9±1.3	2.8±1.1
N20 cortex	2.8±1.6	2.0±1.3
Peakintervals, ms		
N9-N13	3.5±0.4	3.6±0.3
N13-N20	5.8±0.5	6.4±0.4*
N9-N20	9.2±0.5	10.8±0.6*

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

So, in pyramidal syndrome, a slight increase in the latencies of the N13 and N20 components was recorded as compared with the control group. The increase in the latencies of N13 and N20 was symmetrical in most patients in this group, while the latency of the N9 component was relatively unchanged. The amplitude parameters N9, N13, N20 in the group of patients with Chiari malformation 1 were significantly unchanged in comparison with the group of healthy individuals. There was a tendency to a prolongation of the peak-to-peak intervals N13-N20 and N9-N20 in the group of patients with pyramidal syndrome reliably relative to the control. The peak-to-peak interval N9-N13 remained unchanged in the group of patients in comparison with healthy individuals.

Table 11 shows the indicators of somatosensory evoked potentials during stimulation of the tibial nerve in patients with clinical manifestations of pyramidal syndrome.

Table 11: Indices of somatosensory evoked potentials during stimulation of the tibial nerve - latency period, peak amplitudes and inter-peak intervals in healthy individuals of the control group (n = 30) and patients with pyramidal syndrome Chiari malformation 1 (n = 21)

Latency, ms	Controlgroup (n = 30)	Pyramidalsyndrome (n = 21)
N 22 lumbar	23.6±1.9	2.42±1.7
N 30 cervical	30.6±2.5	32.3±2.2**
P37 cortex	37.5±3.4	39.7±3.1*
Amplitude, μV		
N 22 lumbar	1.3±0.5	1.4±0.4
N 30 cervical	0.9±0.3	1.2±0.4*
P37 cortex	2.6±1.5	2.6±1.8*
Peakintervals, ms		
N22-N30	7.62±1.14	7.80±1.05
N30-P37	8.05±1.32	9.5±1.40*
N22-P37	15.7±1.65	16.4±1.5*

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

The latency parameters of the components N22, N30, P37 in the group of patients with Chiari malformation 1 were practically unchanged in comparison with the control group. An isolated expansion of the P37 component (cortex) was noted in 20% of individuals in this group, which can be explained by reactive involvement of cortical structures. The amplitudes of the components N22, N30, P37 in the group of patients did not differ from the normal values. The peak-to-peak interval N22-P37 (lumbar-cortex) was slightly widened relative to the control group. The MPI values N22-N30, N30-P37 were significantly unchanged compared to the control group. From the above, it follows that pyramidal syndrome with Chiari

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malformation 1, according to somatosensory evoked potentials, is characterized by a slowdown in conduction in the central parts of the somatosensory system of the brain. Delayed afferentation at the pontomedullary level in pyramidal syndrome was a little expected fact in combination with movement disorders, which, in our opinion, is due to widespread functional disorders of the conducting systems at the level of the medulla oblongata.

We conducted a study of electroneuromyography of the data obtained during stimulation of the oculomotor, facial and glossopharyngeal nerves, as well as the median and tibial nerves in patients with clinical manifestations of pyramidal syndrome, which are presented in Table 12.

Table 12: Electroneuromyography indices for the oculomotor, facial, glossopharyngeal, median and tibial nerves in healthy individuals of the control group (n = 30) and patients with pyramidal syndrome Chiari malformation 1 (n = 21)

Control group (n = 30)	SPI, m/s	Amax, μV	Additional pathological waves
Oculomotor nerve	29.4±2.2	1080±105.5	-
Facial nerve	39.5±1.8	1235±126.3	-
Glossopharyngealnerve	42.6±2.0	1860±164.0	-
Mediannerve	61.0±1.7	6254±267.0	-
Tibialnerve	49.6±2.1	7125±745.5	-
Pyramidalsyndrome (n = 21)			
Oculomotornerve	27.1±2.1	1052±104.8	
Facialnerve	36.8±1.75*	1126±120.8*	
Glossopharyngealnerve	40.8±2.4*	1635±158.4*	
Mediannerve	42.6±1.4**	3825±253.9*	
Tibialnerve	30.5±2.5**	4905±462.5*	

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - $P< 0.05$, ** - $P < 0.01$*

As follows from the table above, in the group of patients with pyramidal syndrome, there was a significant tendency towards a decrease in PII in the facial and glossopharyngeal nerves. The velocity parameters of the oculomotor nerve were practically unchanged relative to the control group. The amplitudes of the M-responses obtained during the stimulation of the cranial nerves slightly decreased in the group of patients as compared with the normal values. Such changes were symmetrical in most of the subjects (in 80% of cases) and were caused, in our opinion, by bilateral corticonuclear insufficiency. Attention is drawn to the decrease in efferent SPI parameters when stimulating the nerves of the upper and lower extremities. The values of the speed of motor behavior were significantly reduced in the median and tibial nerves from 2 sides in comparison with the control group. All patients with pyramidal disorders showed a reduction in the maximum amplitude of muscle responses along the median and tibial nerves with significant differences from the group of healthy individuals. No additional pathological waves were recorded during stimulation electroneuromyography from the nerves of the upper and lower extremities.

Thus, electroneuromyography data in pyramidal syndrome in patients with Chiari 1 malformation indicated impaired efferent conduction at the suprasegmental level with a predominant involvement of motor pathways at the level of the inferior bridge and medulla oblongata.

d) Syringomyelitis syndrome in patients with Chiari malformation type 1

We have studied in a comparative aspect the neurophysiological features of the syringomyelitis clinical syndrome in 78 patients with Chiari malformation 1, of whom 52 are women and 26 are men aged 14 to 55 years.

Acoustic stem evoked potentials were performed in all patients of this group, the examination results in comparison with the control group are presented in Table 13.

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Table 13: Indices of acoustic stem evoked potentials - latency period, peak amplitudes and inter-peak intervals in healthy individuals of the control group (n = 30) and patients with syringomyelitis syndrome Chiari malformation 1 (n = 78)

Latent period, ms

Control group (n = 30)	PI	PII	PIII	PIV	PV
S	1.79± 0.16	2.95 ± 0.18	3.94 ± 0.24	5.06 ± 0.22	5.97 ±0.25
D	1.72 ± 0.17	2.98 ± 0.19	3.92 ± 0.22	5.13 ± 0.20	6.02± 0.25
Syringomyelitis syndrome (n = 78)					
S	1.80 ± 0.16	2.94 ± 0.17	4.20 ± 0.21*	5.10± 0.20	6.25± 0.22*
D	1.78 ± 0.16	2.96 ± 0.18	4.24 ± 0.19*	5.14± 0.19	6.30 ±0.24*

Amplitude, μV

Control group (n = 30)	PI	PIII	PV
S	0.286± 0.05	0.262± 0.04	0.368 ±0.06
D	0.282± 0.04	0.265± 0.06	0.338± 0.08
Syringomyelitis syndrome (n = 78)			
S	0.280± 0.05	0.310± 0.04**	0.370 ± 0.04*
D	0.286± 0.04	0.325± 0.05**	0.382 ± 0.06*

Peakintervals, ms

Control group (n = 30)	PI-PIII	PIII-PIV	PI-PV
S	2.19± 0.16	2.06± 0.18	4.38± 0.22
D	2.24± 0.18	2.08± 0.22	4.46± 0.24
Syringomyelitis syndrome (n = 78)			
S	2.30± 0.15	2.36± 0.12*	4.56±0.22**
D	2.84± 0.15	2.42± 0.14*	4.61±0.21**

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

As follows from the above data, in the group of patients with syringomyelitis syndrome, there was a significant tendency to the expansion of the latency of the PIII and PV peaks from 2 sides compared to the control group. Bilateral changes in the latent parameters of PIII and PV were observed in 58 (75%) patients. The latencies of the PI, PII and PII peaks were unchanged relative to normal values. When analyzing the amplitude parameters, attention is drawn to the phenomenon of an increase in the PIII and PV peaks with significant differences with the group of healthy individuals. The increase in amplitudes was symmetrical in 45% of cases and asymmetric in 55% of cases, which often correlated with the asymmetric degree of ectopia of the cerebellar tonsils. In all our observations with syringomyelitis syndrome, a significant expansion of the inter-peak intervals PIII-PIII and PI-PV compared with the control group was noted, and the interval PI-PV changed to a greater extent. Violations of the parameters of MPI PI-PIII in patients of this group were not registered. Thus, the predominant symmetric expansion of the MIP PI-PV in patients with syringomyelitis syndrome indicated a widespread deceleration of conduction at the level of pontomesencephalic structures. The increase in the amplitudes of the peaks PIII and PV, in our opinion, were signs of irritative disturbances of the upper olivary complex and mesencephalic structures.

Somatosensory evoked potentials are of great importance in the diagnosis of syringomyelitis syndrome in patients with Chiari malformation 1. We analyzed the changes in somatosensory evoked potentials in patients of this group, obtained by stimulating the median and tibial nerves. Table 14. shows the results of our studies of somatosensory evoked potentials in syringomyelitis syndrome to stimulation of n.medianus.

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Table 14: Indices of somatosensory evoked potentials during stimulation of the median nerve - latency period, peak amplitudes and inter-peak intervals in healthy controls (n = 30) and patients with syringomyelitis syndrome Chiari malformation 1 (n = 78)

Latency, ms	Controlgroup (n = 30)	Syringomyelitissyndrome (n = 78)
N9 Erba	9.6±0.7	14.4±0.6**
N13 neck	13.2±0.8	20.8±0.8**
N20 cortex	18.8±1.0	21.7±1.1*
Amplitude, μV		
N9 Erba	5.4±2.5	2.0-1.1*
N13 neck	2.9±1.3	1.7±0.8*
N20 cortex	2.8±1.6	2.9±1.5
Peakintervals, ms		
N9-N13	3.5±0.4	6.2±0.5**
N13-N20	5.8±0.5	8.9±1.1**
N9-N20	9.2±0.5	16.8±0.8**

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

As can be seen from the data shown, in patients with Chiari 1 anomaly with syringomyelitis syndrome, reliably significant deviations from the norm in latency indices and amplitudes of components N9, N13, N20 were recorded. The latencies of the N9 and N13 components were significantly increased compared to the control group. In 83% of cases (65 patients), such deviations were asymmetric and did not depend on the degree of ectopia of the cerebellar tonsils. Depression of the amplitudes of the N9 and N13 components was significant in the group of patients with relatively healthy individuals, while the N20 values were practically unchanged compared to normal values. Noteworthy is the significantly significant expansion of the peak-to-peak intervals N9-N13, N13-N20, N9-N20 in the group of patients with syringomyelitis manifestations in relatively healthy individuals. Moreover, MPI N9-N13 and N9-N20 were tightened almost twice as much - up to 6.2ms, 8.9ms, 16.8ms, respectively, from the control values. The expansion of the peak latencies was also asymmetric in 75% of cases.

In table 15. we present the results of somatosensory evoked potentials in patients with syringomyelitis syndrome, Chiari malformation 1, obtained by stimulation of n.tibialis.

Table 15: Indices of somatosensory evoked potentials during stimulation of the tibial nerve - latency period, peak amplitudes and inter-peak intervals in healthy controls (n = 30) and patients with syringomyelitis syndrome Chiari malformation 1 (n = 78)

Latency, ms	Control group (n = 30)	Syringomyelitis syndrome (n = 78)
N 22 lumbar	23.6±1.9	30.4±1.8**
N 30 cervical	30.6±2.5	39.8±1.4**
P37 cortex	37.5±3.4	39.5±1.1*
Amplitude, μV		
N 22 lumbar	1.3±0.5	0.6-0.2**
N 30 cervical	0.9±0.3	0.3-0.2**
P37 cortex	2.6±1.5	0.9-0.1
Peakintervals, ms		
N22-N30	7.62±1.14	18.8±2.3**
N30-P37	8.05±1.32	16.7±0.8**
N22-P37	15.7±1.65	24.4±1.05*

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

The presented data show that the latencies of the N22 and N30 components were significantly increased in the group of patients relative to the control parameters. The latency of the P37 component was relatively unchanged compared to the norm. There was a marked reduction in the amplitudes of the N22 and

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N30 components in comparison with the control group. Depression of the amplitudes of the N22 and N30 components was asymmetric in 65% of cases. Deviations of the P37 amplitude from the normal values were insignificant. The most variable were the parameters of the peak intervals N22-N30, N30-P37, N22-P37. The increase in the latency of the MPI was observed in all patients of this group, significantly compared with the control group. The N22-N30 values were increased to a greater extent when the syringomyelitis cyst was located in the thoracic and cervicothoracic spinal cord. The presence of isolated syringmyelia in the cervical spine was characterized by a significant, relatively healthy person, expansion of the N30-P37, N22-P37 MDI with asymmetry on the sides.

Thus, changes in the indices of somatosensory evoked potentials in patients with clinical manifestations of syringomyelitis syndrome with Chiari malformation 1 indicated a violation of segmental afferentation at the level of the cervical and lumbar regions, indicated functional insufficiency of the proximal spinal roots and posterior regions of the spinal structures at these levels. The delay in the central conduction time during somatosensory evoked potentials for stimulation n.medianus et n.tibialis confirmed the presence of both segmental and conduction disorders with involvement of the pontomedullary level.

We carried out electroneuromyography examination of patients with syringomyelia for Chiari 1 anomaly. We registered motor responses obtained during stimulation from the oculomotor, facial and glossopharyngeal nerves, as well as the median and tibial nerves. The research results are presented in Table 16.

Table 16: Electroneuromyography indices for the oculomotor, facial, glossopharyngeal, median and tibial nerves in healthy controls (n = 30) and patients with syringomyelitis syndrome Chiari malformation 1 (n = 78)

Controlgroup (n = 30)	SPI m/s	Amax, μV	Additionalpathologicalwaves
Oculomotornerve	29.4±2.2	1080±105.5	-
Facialnerve	39.5±1.8	1235±126.3	-
Glossopharyngealnerve	42.6±2.0	1860±164.0	-
Mediannerve	61.0±1.7	6254±267.0	-
Tibialnerve	49.6±2.1	7125±745.5	-
Syringomyelitissyndrome (n = 78)			
Oculomotornerve	29.6±2.1	1075±103.8	
Facialnerve	39.2±1.7	1200±118.5	
Glossopharyngealnerve	41.5±1.9*	1730±160.8*	+
Mediannerve	27.4±2.8**	2286±184.5*	+++
Tibialnerve	32.1±1.9**	3850±435.2*	

*Significant differences in identical indicators between the control group and the group of patients (Student t-test) * - P< 0.05, ** - P < 0.01*

In the study of the cranial nerves, a significant decrease in the speed of the efferent impulse along the glossopharyngeal nerve was noted in comparison with the control group. SPI indices for the oculomotor and facial nerves remained unchanged relative to normal values. The amplitudes of muscle responses during stimulation of the indicated cranial nerves were formed and preserved in comparison with the control. In 42% of cases, an isolated decrease in STI along the efferent fibers of the glossopharyngeal nerve was observed when syringomyelia was localized at the level of the upper cervical segments C1-C2 and indicated reactive irritative processes. The decrease in the speed of the impulse conduction along the motor fibers of the median nerve was significant, more often asymmetric in comparison with the control group, more than two times. In the group of patients with syringomyelitis syndrome, significant depression of the amplitude of the n.medianus M-response was recorded relative to the control group. The phenomenon of the appearance of pathological waves of fibrillation, noted at rest and during stimulation of the median nerve in 30 (38%) patients with cervical syringomyelia, requires attention. The STI values for the motor fibers of the tibial nerve in patients of this group were significantly reduced in comparison with normal values. However, the decrease in SPIEff in the lower extremities was less pronounced than in the upper extremities in 52 (66%) patients of this group. The maximum amplitude of the M-response in tibial muscle groups significantly decreased in syringomyelitis syndrome compared with healthy individuals. In the study of n.tibialis, additional pathological potentials characteristic of segmental disorders were not recorded.

Thus, the presence of mixed segmental disorders at the level of the cervical spine, in severe cases involving the anterior spinal structures, is characteristic of the syringomyelitis syndrome in patients with Chiari 1 anomaly during electroneuromyography studies. Conductive disturbances predominated in the

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lower extremities, were often symmetrical in nature and were caused by functional disturbances both at the level of the cervicothoracic spinal cord and by a slowdown in pontomedullary conduction.

Neurophysiological data have diagnostic value in determining treatment tactics. Moreover, in the preoperative period, the most significant were the dynamic changes of the latent parameters, including acoustic brainstem evoked potentials and somatosensory evoked potentials of indicators, which indicated a violation of functional conductivity at the level of the pons, medulla oblongata or spinal structures. We evaluated the changes in the indicators of evoked potentials by the degree of conduction disturbance:

- Mild irritation and slowing down of efferent and afferent conduction (deviation up to 20% from the norm)
- Moderate - violation of efferent and afferent conduction (deviation 20-50% from the norm)
- Pronounced - partial or complete block of conductivity (deviation more than 50% from the norm).

Based on the data obtained, evoked potentials, then further treatment tactics were built in patients with Chiari malformation of type 1.

IV. Conclusion

1. In cerebellar syndrome in patients with Chiari malformation of type 1, the most significant diagnostic criteria are an increase in the latencies of the PIII and PV components, as well as the PIII-PV MPI according to the data including acoustic stem evoked potentials, indicating a slowing of conduction at the pontomesencephalic level.
2. For bulbar syndrome, the defining neurophysiological indicators are a decrease in SPI along the glossopharyngeal nerve and pathological waves of fibrillation along the hypoglossal nerve, indicating damage to the structures of the medulla oblongata with involvement of the cranial nerve nuclei.
3. Pyramidal syndrome is characterized by impaired efferent conduction along the median and tibial nerves, more often of a symmetric nature, according to electroneuromyography, and an increase in MPI PIII-PV with a study including acoustic brainstem evoked potentials, indicating a lesion of the intersection of the motor pathways at the level of the craniovertebral junction.
4. Syringomyelitis syndrome with Chiari malformation of type 1 has pronounced changes in the latent parameters of N9-N20 components; N22-P37 with somatosensory evoked potentials, which is caused by impaired afferentation at the pontomedullary level.

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13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. 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 for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

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

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

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

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon 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 for 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 of 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 criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to 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 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.



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Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

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

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite 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 approaches 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. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a 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 limit the initial two items to no more than one line each.

Reason for writing the article—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 for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity 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 of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets 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 for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory 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 soundly written procedures segment allows a capable scientist to replicate 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 to give the least amount of information that would permit another capable scientist to replicate 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 section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show 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:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the 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—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and 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.



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Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as 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. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit 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 section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an 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 implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully 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 the prospect, and let it drop at that. Make a decision as to whether each premise is supported or 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 an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of 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 other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

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Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.

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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

INDEX

A

Accompanied · 25, 29, 48, 51, 54
Ambiguous · 13
Arteries · 3

C

Carotid · 11, 13, 14, 15, 17, 18, 22, 23
Cranial · 11, 12, 15, 27, 29, 42

D

Dysentery · 27

E

Eligible · 15
Endovascular · 13

F

Fatalities · 11
Fatigued · 13

G

Gradient · 3

I

Insufficiency · 17
Irritation · 21

K

Khartoum · 1, 25, 29, 39

N

Narrowed · 13, 17
Neighboring · 3, 9

O

Opaque · 25, 30

P

Plaques · 18, 21
Platelet · 17, 20, 21
Preponderance · 9, 10, 11
Prevalent · 2, 4, 5, 10, 11, 41
Protocol · 3
Pulmonary · 25, 27, 43

T

Thrombosis · 7, 13, 15, 17, 18, 19, 20, 21, 22, 23, 27, 29
Tortuous · 18, 20, 21
Transient · 10, 25, 29

V

Vessels · 2, 7, 10, 17, 19, 20, 25, 29, 30



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