Online ISSN : 2249-4618
Print ISSN : 0975-5888
DOI : 10.17406/GJMRA

Global Journal

of Medical Research: A

Neurology & Nervous System

Patients with Spinal Cord Injury

Artificial Intelligence (AI) in Psychiatry

Highlights

An Assessment of Emotional State

Therapeutic Approaches to Dysthymia

Discovering Thoughts, Inventing Future

VOLUME 22 ISSUE 3 VERSION 1.0

Global Journal of Medical Research: A
Neurology and Nervous System

Global Journal of Medical Research: A
Neurology and Nervous System
Volume 22 Issue 3 (Ver. 1.0)

Open Association of Research Society

This is a special issue published in version 1.0 of "Global Journal of Medical Research." By Global Journals Inc.

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Employer Identification Number (EIN):
USA Tax ID: 98-0673427

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Yearly Subscription (Personal & Institutional)
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Contents of the Issue

Global Journal of Medical Research: a
Neurology & Nervous System
Volume 22 Issue 3 Version 1.0 Year 2022
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Artificial Intelligence (AI) in Psychiatry - A Summary

By Saagar S Kulkarni, Rohan S Kulkarni & Kathryn E Lorenz
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Abstract- This bibliographic review appraises Artificial Intelligence (AI) theory's applications in the field of psychiatry. Globally hundreds of millions of people suffer from mental disorders. Hundreds of thousands of people in the world commit suicide and also die from an illicit drug overdose due to addiction. Diagnosis and therapy of psychiatric disorders are complex, and machine/computer diagnostic tools for physicians are urgently needed to bolster their decision-making. This study includes various applications AI/machine learning algorithms in various sub-specialties of psychiatry. AI/ML-based psychiatry offers better value over conventional psychiatry in mood disorders, learning disabilities, children and adolescents' mental illnesses, and substance abuse. However, numerous implementation challenges of AI in clinical psychiatric practice remain.

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GJMR-A Classification: DDC Code: 006.3 LCC Code: Q335

Strictly as per the compliance and regulations of:

Artificial Intelligence (AI) in Psychiatry– A Summary

Saagar S Kulkarni [α], Rohan S Kulkarni [σ] & Kathryn E Lorenz [ρ]

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I. Introduction

The key goal of this paper is to evaluate applications of Artificial Intelligence (AI) and machine learning in the field of psychiatry. The past thirty years have shown rapid progress in the use of AI to medical images based fields of radiology, neurology, pathology, and ophthalmology. In addition, as shown in Figure 1, AI has been an essential tool in various medicine-related applications.

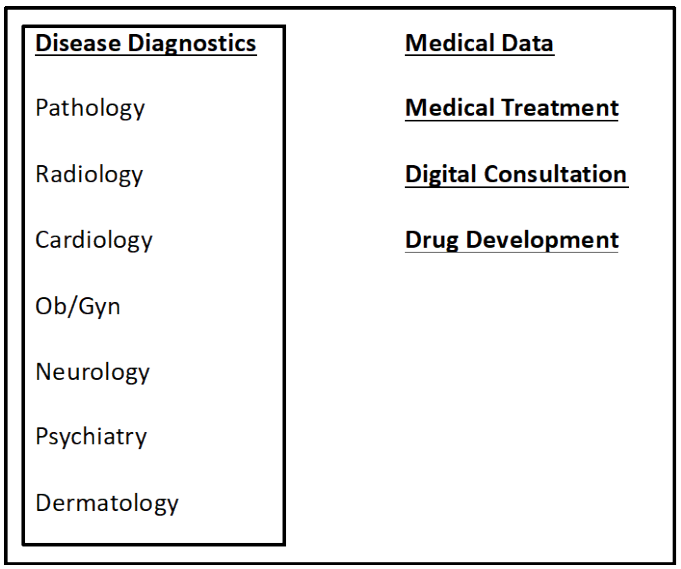

Figure 1: AI in medicine

In the field of psychiatry, as shown in Figure 2, AI has applications in disease determination, categorizing various psychiatric conditions, and various mood disorders.

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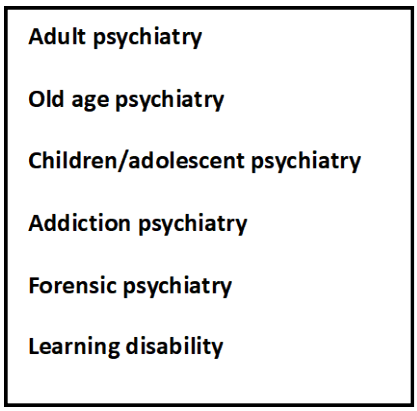

Figure 2: AI in psychiatry

In this article, first we reviewed Artificial Intelligence-based psychiatry research in various clinical situations that are included in Figure 2. Secondly, different ethical and social issues of AI Artificial Intelligence faces for use in psychiatric applications are discussed.

II. Artificial Intelligence or AI

By definition, Artificial Intelligence or AI is an intelligence that is not natural or is artificial. AI is founded on various statistical principles where a phenomenon is 'learned' by a machine. The phenomenon gets cleverer as more learning of it is managed. After a suitable quantity of this training, then, AI can be, as a human being, useful for making decisions. In this section important AI terms and ML-based algorithms are explained.

a) AI basics

In this section, important AI terms are briefly discussed.

Machine learning (ML) approach pools statistical modeling and computers together to learn from available data. ML is characterized into 'supervised' and 'unsupervised' learning.

i. Supervised learning method builds a forecast model of a known output and input data set. The model is then utilized to predict new output given new output information. This approach is well suited for both i) 'classification' model for output categories (e.g., a patient has an illness or patient does notis based on an MRI scan) and ii) 'regression' model where the output variable is continuous (e.g., patient's weight).
ii. Unsupervised learning approach groups data together, to comprehend the intrinsic structure of the data, based on their resemblances and when there is no output prediction variable and input data is not labeled. E.g., clustering patterns in a sample of patients with an illness that could lead to new drug therapy.
iii. Semi-supervised learning is a blend of 'Supervised' and 'Unsupervised' learning approaches (e.g., conglomerate algorithms of 'classification' and 'clustering').

Artificial Neural Networks or ANNs attains an output forecast that results from numerous independent phases of computations and weightings. ANN, similar to a neuron network in a brain, has a set of artificial layered/connected neurons to transfer data through the web.

b) ML algorithms

Supervised Machine Learning modeling involves the splitting the available information into both 'training' (or 'educating') and 'testing' data sets for verification. In Supervised ML, the following algorithms are extensively utilized:

A. Regression: For ML, both 'Linear regression' (use of least squares regression line with the lowest error among the cause/independent variables and the effect/dependent variables), and 'Logistic Regression' (used for binary outcomes of 'yes/no,' or 'no illness/illness' with forecasters types of either categorical or continuous) methods are commonly used based on data characteristics.
B. Decision Tree (DT): The decision tree-based ML algorithm includes a set of rules that describes the pathway from the root to the leaves. The feature of interest is analyzed at the node while the output of the analysis is assigned at the branch.
C. Naive Bayes: ML algorithm based on Naive Bayes postulates that the characters under assessment are independent of each other.
D. Support Vector Machine (SVM): The Support Vector Machine-based ML algorithm finds a nonlinear relationship and categorizes data by describing a hyper plane that best distinguishes the existence of two groups.
E. *k*-Nearest Neighbor (*k*-NN): '*k*-Nearest Neighbor' based ML algorithm is utilized for data categorization of nonparametric grouping. The '*k*' is defined as the square root of the number of incidences and its remoteness from a pre-selected

point. Moreover, the categorization is established on the number of *k* neighbors.

F. Random Forest (RF): ML with Random Forest algorithm, which prevents 'overfitting,' is an efficient tool for an accurate estimate of classifiers. Nevertheless, the RF-based ML algorithms are less proficient than the SVM/or *k*-NN/logistic regression-based ML methods.

G. Convolutional Neural Networks (CNNs): 'Convolution' is a form of a mathematical function on two functions that produces a third function. Convolutional Neural Networks, feed-forward networks, learn by using numerous layers of nodes and several replications of both 'analyzing' and 'weighting' the patterns it recognizes in the images. The value/size of weights is decided based on how correctly it classifies a design or structure.

III. AI in Mood Disorders

Health professionals use 'mood disorder, 'a mental health category, to generally label all categories of depression and bipolar disorders. However, a significant overlap in symptoms exists between these disorders. This is where AI and machine learning come into play with their potential to improve the accuracy of diagnosing different mood disorders.

a) AI in depression

Having less concern in everyday activities, feeling unhappy or miserable, and other similar indications for minimum two weeks may signal depression.

In 2020, Richter et al. research focused on a novel methodology to assess for dissimilarities in cognitive prejudices amid subclinical depressed and anxious persons. They, based on the stages of depression and anxiety indications, separated 125 people into four groups. A wide-ranging behavioral examination sequence revealed and measured numerous 'cognitive–emotional' biases. The authors developed sophisticated machine learning (ML) tools to scrutinize these outcomes. These techniques uncovered distinctive configurations that differentiate depression against anxiety. The model distinguished well between symptomatic members (with high signs of depression, anxiety, or both anxiety) compared to the control group with no symptoms. It resulted in a 71.44% classification prediction accuracy (sensitivity) for 'high anxiety/high depression/high anxiety and high depression' and 70.78% classification prediction accuracy(specificity) for 'low anxiety and low depression. 'In addition, the model yielded in classification prediction accuracy of 68% for 'high depression' while74.18% for 'high anxiety.'[1]

Li et al. in 2019usedelectroencephalogram (or EEG to detect electrical activity in the brain using small, metal electrodes attached to the patient's scalp) and ML to better diagnose depression amongst 28 individuals. The Mini-International Neuropsychiatric Interview (MINI) approach was utilized by the physicians as the measure by the authors for the identification of depression. Original features of 'power spectral density' and 'activity' were individually obtained by means of auto-regress model' and the Hjorth algorithm with specific time frames. Two distinct methods of 'ensemble learning' and 'deep learning' processed these features. The ensemble learning used a deep forest transformation of the original features to new and a support vector machine (SVM) as a classifier. In the deep learning method, the authors added spatial data of EEG caps to both features and implemented Convolutional Neural Network (CNN) for recognition. Their approach yielded accuracy of 89% using the ensemble model and power spectral density. The deep learning method achieved 84.75% accuracy using the activity. The research showed that EEG could be utilized as a dependable gauge for recognizing depression.[2]

In 2018, Dinga et al.'s work assessed the predictive value of a varied range of clinical, biological, and psychological features for forecasting the progression of depression and targeted to detect the top predictors. The authors evaluated 804patients with dysthymia or unipolar depression involving 81 of these features. The patients were clinically monitored for two years. The patients, applying a latent class growth analysis, were grouped into (i) the presence or lack of a depression, and (ii) disease course trajectory groups of rapid remission, gradual improvement, and chronic. The authors used a 'penalized logistic regression' to forecast depression progression and to also assess the predictive magnitude of distinct variables. They, established on the inventory of depressive symptomatology (IDS), estimated a swift reduction course of depression with an area under the Receiver Operating Characteristic (ROC) curve of 0.69 with 62% accuracy. Also, at follow-up, the existence of an MDD identification presented an area under ROC of 0.66 and 66% accuracy. Out of the sizeable set of considered parameters, only the IDS offered prognostic magnitude for course forecast on an individual level. Though the accuracy of course prediction was moderate at best.[3]

Chekroud et al. in 2016,came up with a procedure to evaluate whether patients with depression will attain symptomatic reduction from a twelve-week treatment of an antidepressant such as citalopram. The authors used self-reported data from 1,941 patients with depression from 'ClinicalTrials.gov'(number NCT00021528) to detect variables with the highest predictive of medical treatment results. They utilized these variables for training an ML model to forecast clinical depression remission. This model was externally confirmed by them in the escitalopram treatment group of 151 patients from a separate clinical trial (number NCT00590863). The ML model was trained with 25 self-reported variables, with the most predictive of treatment

outcome, from 164 patients. The model, after internal cross-validation, predicted outcomes with an accuracy of 64·6% with $p<0·0001$. The external validation of the 151 patients from the escitalopram treatment group attained an accuracy of 59·6% with $p=0.043$. The model, when applied to a combined escitalopram-bupropion treatment group of134 patients, resulted in an accuracy of 59·7% with $p=0·023$.However, when used for a combined venlafaxine-mirtazapine group of 140, the model displayed an accuracy of 51·4% with $p=0·53$, suggesting the model's specificity to core mechanisms. The authors showed that use of the ML models by extracting available clinical test data can allow potential identification of patients prone to have a positive response to a specific antidepressant.[4]

In 2015, Patel et al., for accurate diagnosis and treatment of depression, studied numerous ML approaches with 'multi-modal imaging' and 'non-imaging' whole brain and network-based features as inputs. The authors recruited 33 older depressed and 35 late-life non-depressed individuals. Their demographics and cognitive ability scores were first documented, followed by attainment of their brain characteristics using multi-modal MRI. Linear and nonlinear ML methods were then examined by the authors for appraising models' predictive accuracy. An 'alternating decision trees' method projected the highest accurate forecast models for late-life depression diagnosis with 87.27% accuracy, while the treatment response attained 89.47% accuracy. The diagnosis model included measures of age, Mini-mental state examination score, and structural imaging (e.g., whole brain atrophy and global white mater hyperintensity burden). The treatment response model included measures of structural and functional connectivity. Thus multi-modal imaging coupled with a 'non-imaging' methods-based approach can predict depression diagnosis and treatment response for older age patients and allow custom-made depression treatment for them.[5]

In 2013, Hosseinifard et al. 'swork demonstrated, based on 45 un-medicated depressed patients and 45 normal subjects, that nonlinear analysis of EEG is valuable method for discerning depressed patients and control subjects. From the EEG signal, the authors extracted four nonlinear features (Lyapunov exponent, Higuchi fractal, detrended fluctuation analysis, and correlation dimension. For differentiating the two groups, the authors, as the classifiers, used 'k-nearest neighbor, ''linear discriminant analysis' and 'logistic regression. 'The highest classification accuracy of 83.3% was achieved by correlation dimension and LR classifier. The authors improved their model when all nonlinear features were collectively applied to classifiers yielding a classification accuracy of 90% by LR classifier and all nonlinear features.[6]

b) AI in bipolar disorders(BD) and schizophrenia (SZ)

Bipolar disorder is a circumstance when a person has phases of depression interchanging with phases of raised mood ormania. In comparison, an individual with schizophrenia interprets reality abnormally and has two or more symptoms out of: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms.

Tomasik et al. in 2021, based on blood biomarker data and an online questionnaire, developed a diagnostic algorithm to decrease the misidentification of 'Bipolar Disorder' (BD) as 'Major Depressive Disorder' (MDD). Their model utilized data from patients aged 18-45 years with depressive symptoms. In order to establish their depression diagnosis, phone interviews were conducted after patients answered an online questionnaires and provided dried blood samples for biomarker assessment. The authors applied 'Extreme Gradient Boosting 'followed by nested cross-validation to train and validate models distinguishing BD from MDD in individuals who self-described diagnosis of MDD. The area under the ROC curve for splitting participants with 'BD diagnosed as MDD' from those with 'truthful MDD' was 0.92 with a 95% Confidence Interval of 0.86–0.97.Validation in cases of participants without previous diagnosis of mood disorder diagnosis produced area under the ROC of 0.89 and 0.90 for distinguishing newly identified BD and subclinical low mood from MDD, respectively. Validation in participants with previous BD identification showed 86% sensitivity. The authors' algorithm thus accurately recognized patients with BD in numerous clinical circumstances, which could assist in accurate clinical identification and management of BD.[7]

In 2021, Siqueira Rotenberg et al.'s research analyzed ML approaches as a likely forecaster in BD-related depressive relapses. The authors applied ML algorithms of RF, SVM, Multilayer Perceptron, and Naïve Bayes, to a group of 800 patients (507 with depressive relapses and the remaining 293 without). The ML algorithms' prediction ranged between 61 and 80% in terms of F-measure. The RF approach's performance was the best, with 68% for a relapse cohort and 74% without. Thus, ML algorithms can assist in clinical decision-making for patients requiring BD management.[8]

Fernandes et al. in 2020, using immune and inflammatory biomarkers in peripheral blood and cognitive biomarkers utilizing ML, established a model with probabilistic multi-domain data integration in order to predict the identification of BD and schizophrenia(SZ) based on 416 participants. Their model for 'with the BD' vs. 'without' displayed a sensitivity of 80% and specificity of 71%. For ' with the SZ' vs. 'without', the model produced sensitivity and specificity of 84% and 81%, respectively. However, the model was moderately

effective for the discriminating between BD and SZ with a sensitivity of 71% and specificity of 73%.[9]

In 2019, Belizario et al. work focused on understanding if Predominant polarity (PP) is a vital specifier of BD. The authors applied ML algorithms to establish a patient´s PP but without including the number and polarity of past incidents, and searched for the links between PP and demographic/clinical factors. Clinical and demographic characteristics were gathered from 148 BD patients using a tailored questionnaire. The authors utilized the RF algorithm to categorize patients into either 'depressive' or 'manic 'PP and uncover which factors were linked to the specifier.

The model produced an area under the ROC curve of 74.72% in categorizing patients into either 'depressive' or 'manic' PP. The top factors selected by the model included: age at the first depressive episode, number of hospitalizations, BD Type II, manic onset, and delusions. Additionally, anxiety disorders, alcohol dependence, eating disorders, and substance dependence appeared to be linked with PP. The research work demonstrated that the ML could assist in a patient's PP diagnosis.[10]

In 2018 Perez Arribas et al. applied a 'signature-based' learning method to a cohort of 130 participants (48 with BD, 31 with borderline personality disorder, and 51 control) who, using a bespoke smartphone app, daily submitted for one-year mood ratings. The model was used to record the progressing interrelations amongst the distinctive features of mood and use this information to categorize participants' diagnosis and to forecast succeeding mood status. The model could differentiate amongst the three participant cohorts, with categorization accuracy of classified 75% into the correct diagnostic cohort versus with 54% utilizing standard methods. Additionally, succeeding mood scores were accurately forecasted with higher than70% accuracy. The forecast of mood was most accurate in the control group (89–98%), followed by bipolar disorder (82–90%) and borderline personality disorder (70–78%). The authors thus successfully demonstrated the signature method to analyze mood data in terms of diagnostic classification and prediction of future mood.[11]

Schnack et al. in 2014 work focused on utilizing MRI scans to distinguish SZ from BD. Their study included scans, using a 1.5 T MRI scanner, of 198 participants (66 each with SZ, with BD, and the healthy/control). Three SVMs, based on their gray matter density images, were trained to distinguish patients with SZ from the control group, patients with SZ from those with BD, and patients with BD from the control cohort. The model separated a) SZ patients from BD patients with an accuracy of 88%, and b) patients with SZ from control participants with an accuracy of 90%. The approach was moderately accurate is separating BD patients from the control cohort with correct categorization (accuracy for BD 53% and control 67%). Application of 1.5 T MRI scanner-based models on a validation set from a 3 T MRI scanner provided average categorization accuracies of 76% (control vs.SZ), 66% (BD vs.SZ), and 61% (control vs.BD).This research work, based on structural MRI scans, showed that the accurate separation of SZ from BD using gray matter pathology caould aid in the differential diagnosis of these disorders.[12]

c) AI in suicidality with mood disorders

Suicide, an individual taking their own life, is a catastrophic response to traumatic life circumstances. A majority of all suicides are by individuals who agonize from mood disorders. Thus, avoidance of suicide among those who suffer from mood disorders is a key to preventing a suicide.

In 2021 Hong et al.'s research assessed a group of 66 adolescents and young adults with MDD diagnosis. They obtained T1-weighted MRI scans which then were categorized utilizing the SVM algorithm to separate 'suicide attempters' from people with 'suicidal ideation but without attempts. 'Their model identified' suicide attempters' and individuals with 'suicidal ideation but without attempts' with an accuracy of 78.59%, the sensitivity of 73.17%, and specificity of 84.0%. For the 'suicide attempters,' the Positive Predictive Value (PPV) of suicide attempts was 88.24%, while the Negative Predictive Value (NPV) was 65.63%. The authors were able to derive the top 10 ranked classifiers for a suicide attempts. The outcomes of this research specified that structural MRI-based information could be beneficial for the categorization of suicide possibility among MDD patients.[13]

Agne et al. in 2020 work focused on understanding the reasons why patients with obsessive-compulsive disorder (OCD) have a higher risk of suicide attempts vs. the general population. The authors used the ML method to find out if the driver(s) of the higher suicide attempts include the sociodemographic factors and comorbidities. The analysis included 959 patients with OCD using an elastic net model to identify the forecasters of suicide attempts utilizing sociodemographic and clinical factors. The occurrence of suicide attempts in the sample authors studied was 10.8%. The model yielded a) previous suicide planning, b) previous suicide thoughts, c) lifetime depressive episodes, and d) intermittent explosive disorder as relevant predictors of suicide attempts. The elastic net model with an area under the curve of 0.95 thus provided a high accuracy performance algorithm.[14]

In 2019, Carson et al. developed a ML algorithm utilizing natural language processing of electronic health records to detect suicidal conduct among youths those are hospitalized for psychiatric issues. A total of 73 individuals from the northeastern US, with an electronic health record, available before hospitalization, who responded to a survey fora record of suicide attempts in

the past year before the hospitalization were selected for this study. The clinical notes from these records prior to inpatient admission were processed for phrases linked with the suicide attempt. The authors then applied the RF machine learning approach to develop a categorization model. The model demonstratedi) a sensitivity of 0.83, ii) specificity of 0.22, iii) area under the curve of 0.68, iv) a PPV of 0.42, v) NPV of 0.67, and vi) an accuracy of 0.47. The phrases highly linked with suicide attempts are grouped around terms related to suicide, psychotropic medications, psychiatric disorders, and family members. This research thus displayed a reasonable achievement of a natural language processing method in the identification of suicide attempts among hospitalized youths with a psychiatric background.[15]

In 2017, Jihoon et al.'s work focused on if the data from multiple clinical scales have categorization power for detecting actual suicide attempts. Five hundred seventy-three participants with disorders of depression and anxiety completed questionnaires, including 31 psychiatric scales, concerning their record of suicide attempts. The authors first trained an ANN classifier with total of 41 factors (31 psychiatric scales and ten sociodemographic factors), followed by a ranking of the impact of each factor on the categorization of suicide attempts. The model demonstrated an accuracy of detecting suicide attempts of 94% in one month, 91% in one year, and 87% in a lifetime. The areas under the ROC curves for suicide attempts detection were 0.93 for one month, 0.87 for one year, and 0.89 for a lifetime. The questionnaire regarding 'Emotion Regulation' had the highest impact among all factors. This ML-based research thus demonstrated that self-reported clinical scales could be valuable for the categorizing of suicide attempts.[16]

Passos et al.'s study in 2016looked at various clinical risk variables to calculate the likelihood of an individual attempting suicide. Demographic and clinical variables based data from 144 patients, who were diagnosed with a mood disorder, was used for training an ML algorithm. This algorithm was then used by the authors in classifying new individuals as either 'suicide attempters' or 'non-attempters.' Three different ML algorithms were applied and assessed. All these algorithms separated' suicide attempters' from 'non-attempters' with forecast accuracy ranging from 65% to 72% with p value <0.05. The Relevance Vector Machine (RVM) algorithm correctly forecasted the behavior of 103 of the 144 subjects producing 72% accuracy and an AOC of 0.77 with a p-value <0.0001. The critical predictor factors in discriminating 'suicide attempters' from 'non-attempters' comprised of a) prior hospitalizations for depression, b) a record of psychosis, c) cocaine dependency, and d) posttraumatic stress disorder. Thus, the authors were able to identify demographic and clinical risk factors for suicide attempts in individuals with mood disorders.[17]

d) AI in Addiction

Despite harmful consequences, uncontrolled consumption of either a substance (e.g., drugs, alcohol, food) or a medium (e.g., technology). The person's capacity to function in day-to-day life can become compromised with addiction even though the individuals know the habit is producing or will produce complications.

In 2021, Gao et al.'s study focused on a 'proteome-informed' ML algorithm to uncover an almost ideal compounds for anti-cocaine dependence. The authors using 32 ML different models, performed over 60K experimental drugs for side effects and re-purposing possibilities. All of the current drug candidates did fail in both cross-target and Absorption/Distribution/Metabolism/Excretion/Toxicity (ADMET) screenings. However, the ML algorithms recognized numerous' nearly optimum' possibilities for additional optimization.[18]

Choi et al.'s research in 2021aimed to categorize predictor factors (e.g., environmental causes, social, and mental) that produce nicotine dependence in youth who consume e-cigarette or hookah consumers and construct nicotine dependence forecast models using ML algorithms of a) RF with Relief F and b) Least Absolute Shrinkage and Selection Operator or LASSO. These ML-based prediction models utilized data from the 2019 National Youth Tobacco Survey participants of 6,511 who were recognized as ever consumed either e-cigarettes or hookah. A final analysis based on 193 predictor factors showed a) witnessed e-cigarette use in their household, and b) perception of their tobacco use as top factors that could be utilized in public alertness for policymakers.[19]

In 2021 Wang et al.'s work focused on developing SVM models to recognize internet addiction and evaluate the effectiveness of cognitive behavior therapy (CBT) founded on 'unbiased functional connectivity density or FCD. 'Total of 57 participants (27 with IA and 30 with healthy control or HC) provided resting-state fMRI before and after eight-week CBT meetings. The discriminatory FCDs were calculated as the characters of the support vector classification model to identify persons with IAs from the HCs. The authors' model effectively separated participants with IA with an accuracy of 82.5% from HCs with an area under the curve of 0.91.Furthermore, FCDs of potential neuroimaging biomarkers for IA were confirmed as a) hyperactive-impulsive habit system, b) hypoactive-reflecting system, and c) sensitive interoceptive reward awareness system.[20]

In 2019, Symons et al.'s research efforts analyzed the performance of ML models vs. medical professionals to forecast alcohol addiction results in

patients after CBT. Twenty-eight ML models were built and trained utilizing a) demographic and b) psychometric assessment data from 780 patients who had gone through a 12-week, abstinence-based CBT program for alcohol addiction. Additional 50 patients for prediction were assessed by i) ten addiction therapy experts, and with ii) twenty-eight trained ML models. The highest accuracy ML model of 74%was far superior vs. the four least accurate therapists, with 51% to 40% accuracy. However, the model's robustness was low as the area under the ROC curve was only 0.49. The mean aggregate predictive accuracy of these 28 ML models was slightly better (58.6%) than the ten clinical therapists (56.1%). Thus the research showed that the highest performing prediction models have the potential to help the therapists in clinical settings.[21]

IV. AI in Forensic Psychiatry

Forensic psychiatry tends toward a heavy emphasis on science, and forensic psychiatrists identify and handle mental disorders in the framework of the criminal judicial system.

In 2022, Hoffmann et al., using ML methods, explored aggression in 370 offender inpatients with schizophrenia spectrum disorders (SSDs). The SVM based models yielded the best accuracy out of all ML models, with an accuracy of 77.6% and an area under the ROC curve of 0.87.The most predictive factors in separating 'aggressive' from 'non-aggressive' in inpatients were a) negative behavior toward other patients, b) the breaking of ward rules, c) the positive and negative syndrome (PANSS) score at admittance, d) poor impulse control and impulsivity. This research is a good example of ML's usefulness in forensic psychiatric research related to aggression in SSD.[22]

In 2021 Watts et al. applied ML techniques to predict the type of criminal wrongdoings in psychiatry patients, at an individual level. Multiple ML models (Random Forest, Elastic Net, SVM) were built and trained based on 1,240 patients in the forensic psychiatric health system. Using only 36 clinical factors, sexual crimes were forecasted by the authors, from both 'non-violent' and 'violent' offenses with a sensitivity of 82.4% and specificity of 60.0%. The authors, utilizing a binary classification model with 20 clinical factors, forecasted sexual and violent acts, with 83.3% sensitivity and 77.4% specificity. Furthermore, using 30 clinical factors, non-violent and sexual offenses can be separately forecasted with 74.6% sensitivity and 80.7% specificity. These results indicate that ML models can display higher accuracy than the current risk assessment tools (which also cannot individually predict) with the area under the ROC curves between 0.70 and 0.80. However, a considerable subset of patients in this analysis had a history in the criminal system preceding an official diagnosis. Thus, many of the factors that forecast these behaviors might result from the problems of past offenses.[23]

Philipp et al., in 2020, using ML, investigated 569 predictor factors for their forecasting power for either 'coercion' or 'no coercion' in 358 patients (131 who did experience coercion while 227 who did not).The data was split (70/30%) first to find the best ML model (70% of data) and the remainder data (30%) for extracting most essential factors from the best model found. The best model had a balanced accuracy of 73.3% and an area under the ROC curve (a predictive power) of 0.85 with the top five prediction factors of a) threat of violence, b) actual violence toward others, c) the application of direct coercive measures during past psychiatric inpatient treatments, d) the PANSS poor impulse control, e) uncooperativeness, and hostility. This research confirmed prior discoveries and added detail on variables revealing the use of coercion.[24]

V. AI in Personality Disorders

Kinds of personality disorders are categorized into three groups/clusters, founded on similar features and indications. These personality disorders are:

a) Cluster A is categorized by odd, eccentric thought processes and, or conduct,
b) Cluster B is categorized by the overly emotional thought processes and, or unpredictable conduct,
c) Cluster C is categorized by anxious, fearful thought processes and, or conduct.

In 2014, Randa et al. builtan 'expert system,' which mimics the 'expert rational' in deciphering a problem, of personality disorders to help assist in the early identification of the illness. The authors used a 'Certainty Factor' method to estimate the likelihood of someone is suffering from this illness. They demonstrated an approach to establishing the types of personality disorders founded on symptoms experienced. Their calculations based on the method of Certainty Factor displayed a 77.2% confidence level.[25]

Berdahl, in 2010, developed a framework for etiology of Borderline Personality Disorder (BPD) by building a NN with restrictions from a) neuroanatomy, b) neurophysiology, and c) behavior. The NN models showed how various brain make-ups could interrelate during BPD. These NN simulations indicated that long-term depression (LTD) in the brain structures might clarify various BPD symptoms.[26]

Hayat et al. in 2019 investigated aback propagation neural network (BPPN) model for the early discovery of type B personal disorder. The model used 43 data points for training and 34 for testing. The model's output was cataloged into four identification classifications of type B personal disorder: i) anti-social, ii) borderline, iii) histrionic, and iv) narcissistic. The model achieved an accuracy of 90.7% in training and 97.2% in testing. The authors thus showed a high

accuracy BPPN model to diagnose type B personal disorder.[27]

VI. AI in Child and Adolescent Psychiatry

The child and adolescent psychiatric fields focus on the identification and the management of disorders of i) thinking, and ii) feeling and, or behavior disturbing children, adolescents, and their families.

In 2022 Dobias et al. utilized individual sociodemographic factors and depression symptoms as predictors to study the capacity to forecast 'whether' and 'where' adolescents (ages 12-17) get mental healthcare. The authors analyzed data from the 2017 National Survey of Drug Use and Health as a characteristic sample of non-institutionalized individuals in the US. The analysis included both RF and elastic net-based ML models. The model's assessment was based on data from total of 1,671 youths (inpatient, outpatient, and other) with raised depressive symptoms. Only 53% of these youths sought care of any kind. Using the two predictors, the RF models explained no 'pseudo- out-of-sample' deviance in youth accessing any depression treatment, while elastic net models performed slightly better, explaining 0.80–2.50% 'pseudo-out-of-sample' deviance for access to all depression treatments. This research thus showed considerable limits in our ability to forecast 'whether' and 'where' youths access mental healthcare.[28]

Haque et al.'s research in 2021focused on ML algorithms for detecting depression among children and, or youths aged four to17 years and factors that contribute to the illness. In this research, for modeling, multiple available datasets from 2013-14 for the Australian children and youths were used. In the depression recognition step, MF algorithms based on RF, XGBoost, Decision Tree, and Gaussian Naive Bayes were used. The RF-based ML algorithm was the best in forecasting depressed categories by 99% with an accuracy of 95%.[29]

In 2021, Price et al. studied the association between childhood maltreatment and structural alterations in the brain.

They utilized ML based on elastic net regularized regression to detect if and how brain structure differed among young adults (18-21 years of age) with and without a record of mistreatment. A total of 384 individuals completed an evaluation of juvenile trauma experience and a structural MRI. A model which included five subcortical volumes, seven cortical thicknesses, and 15 surface areas yielded an area under the ROC curve of 0.71 with a p-value less than 0.001. The individuals with a mistreatment past had smaller surface areas and cortical thicknesses predominantly in 'frontotemporal' areas. They also displayed more enormous cortical thicknesses in occipital regions and larger surface areas in frontal regions. This research clearly demonstrated that childhood abuse is associated with numerous measures of structure in the brain.[30]

To diagnose anxiety and depression, McGinnis et al. in 2018 proposed the application of a 90-second fear induction task during which time an individual's motion is monitored using a wearable sensor that is commercially available. In contrast, current diagnostic approaches for detecting the illness takes days. A multitude of ML models was utilized by the authors to extract from one 20-second phase of the task to forecast diagnosis. The best model demonstrated a diagnostic accuracy of 75%, comparable to current diagnostic methods, however, at a relatively insignificant fraction of the time and cost.[31]

In 2017 Saxe et al. studied if ML methods can generate predictive categorization models for childhood Posttraumatic Stress Disorder (PTSD) and also if explicit factors can be recognized for the disorder. The authors applied ML forecasting categorization methods to 105 biopsychosocial risk variables. The variables were based on data which was collected from 163 injured hospitalized children that were diagnosed with PTSD three months after their discharge. A forecasting categorization model was realized by the authors with meaningful accuracy. A model built based on subsets of possibly causally relevant characters achieved similar forecasting ability paralleled to the best model constructed with all factors. The authors found that the Causal Discovery Character Choice-based methods recognized 58 factors, of which ten were classified as very stable. Thus authors using ML algorithms could establish both forecasting categorization models for childhood PTSD and categorize numerous causal factors.[32]

VII. AI in Attention Deficit Hyperactivity Disorder (ADHD)

An individual with attention deficit hyperactivity disorder (ADHD) condition has differentiations in brain development and brain activity, from a normal brain, which disturbs attention, the ability to sit static, and self-discipline. It is critical to diagnose children with displaying substantial losses and symptoms of ADHD at an early age as early detection and treatment may lead to more effective, and shorter treatment.

In 2011, Delavarian et al. explored the use of AI in diagnosing children with different behavioral disorders. By using the Matlab toolbox for pattern recognition known as "Prtools," the authors examined a total of 16 different classifiers and their accuracies in differentiating between childhood conditions that present with similar symptoms. The specific disorders included ADHD, depression, anxiety, comorbid depression and anxiety, and conduct disorder (i.e., the

outputs). The study involved 306 children, and 38 common symptoms of childhood behavioral disorders were used as inputs. The authors concluded, from the data collected, that the nearest mean classifier was the most accurate classifier, with an accuracy of 96.92%. Not only was it the most accurate of the classifiers examined, but it was also significantly more accurate in diagnosing children with behavioral disorders compared to not using a classifier at all (87.51%). The authors showed that the use of specific classifiers can help aid in improving the correct diagnosis of childhood behavioral disorders. This is key, as correctly identifying patients with these disorders at earlier stages in life will allow for earlier interventions and subsequently improved outcomes.[33]

In 2010, Anuradha et al.'s research applied the SVM Algorithm in diagnosing ADHD. The Support Vector Machines are a frequently utilized artificial intelligence technique; by constructing a hyperplane or sets of hyperplanes in a high-dimensional space, the authors used this technique to classify a group of 100 children, ages 7-10 years old, as either having or not having ADHD. The input to the SVM Algorithm was primarily in the form of answers to a questionnaire. The questionnaire consisted of 6 yes-or-no questions, with values of 1 given to "yes" answers and 0 assigned to "no" answers. After the input data was fed into the Algorithm, the output was recorded as either "1" for diagnosis of ADHD or "0" for no diagnosis of ADHD. According to the data reported in this study, the SVM Algorithm was correct in diagnosing/not diagnosing ADHD 88.7% of the time when comparing the output from the Algorithm to the diagnoses made by trained physicians. (While this study design assumes that the physicians are correct in their diagnoses, it is promising that this Algorithm can match the diagnosis of trained physicians nearly 90% of the time).[34]

Ariyarathne et al. in 2020, based on a CNN model, proposed using fMRI data of the "resting brain" in conjunction with seed-based correlation analysis to classify and identify children with ADHD. Seed-based correlation analysis works by computing the functional connectivity between different regions within the brain. Four specific brain regions were studied, including the Medial Prefrontal Cortex (MPC), Posterior Cingulate Cortex (PCC), Left Temporoparietal Junction (LT), and Right Temporoparietal Junction (RT). From the seed-based correlation analysis of these brain regions, a Convolution Neural Network (CNN) was used as a pattern recognition classifier to distinguish between patients with ADHD and patients without ADHD (controls). According to the results, the accuracy of classification of patients with ADHD was highest in the Medial Prefrontal Cortex (MPC) region of the brain at 85.21%. This should not come as a surprise, claimed the researchers, as the primary region of the brain implicated with ADHD is the prefrontal cortex.[35]

VIII. AI in Geriatric Psychiatry

Geriatric psychiatry, the practice of psychiatry in older adults, is a vital field of psychiatry. Many of aging related body changes (e.g., blood and nervous system) might escalate an individual's probability to suffer depression, mental impairment, and dementia.

In 2021 Yadgir et al.'s study focused on ways to categorizing patients, aged above 59 years, with a high risk of Cognitive Impairment (CI) using ML-based on factors accessible from electronic health records (EHRs).The authors used records of 1,736 adults who were dismissed from three emergency departments (EDs). Each adult's CI was estimated by the authors, based on the 'Blessed Orientation Memory Concentration' (BOMC) test conducted in the ED. A 'nested cross-validation' framework was utilized to assess ML algorithms. Using BOMC scores, 121 (7% of 1,736) adults tested positive for potential CI. The top-performing ML algorithm, of XGBoost, forecasted BOMC positivity with an area under the ROC curve of 0.72. With a categorization threshold of 0.4, the model yielded 0.73 sensitivity, 0.64specificity, an NPV of 0.97, and a PPV of 0.13. This work showed that an ML algorithm built on EHR data could separate patients at higher risk for CI.[36]

Hemrungrojn et al., using a neural network algorithm, in 2021, looked at the Thai population for the categorization of amnestic mild cognitive impairment (aMCI) and Alzheimer's disease (AD). The authors used Montreal Cognitive Assessment (MoCA) to study incorporated 60 AD patients, 61 aMCI patients, and 60 healthy controls (HCs).The authors, using their model, discriminated against a MCI patients from AD patients with an area under the ROC curve of 0.94, and HC with an area under the ROC curve of 0.81.The ML method exhibited that i) 'aberrations in recall' was the most significant feature of a MCI vs. HC, and ii) 'aberrations in visuospatial skills' and 'executive functions' were the top features of AD versus a MCI. Furthermore, impairments in a) recall, b) language, and c) orientation distinguished AD from a MCI. However, d) attention, e) concentration, and f) working memory did not. Thus the authors demonstrated that the ML algorithm based on 'MoCA' is a suitable cognitive assessment tool for the Thai population for the identification of a MCI and AD.[37]

In 2019 Facal et al.'s research explored the effect of cognitive reserve (CR) in transforming from mild cognitive impairment (MCI) to dementia using both traditional and ML-based approaches. Using Petersen criteria for diagnosis, 169 participants who completed the longitudinal study were divided into three MCI subgroups, and a healthy control group. The authors utilized nine ML categorization algorithms to analyze collected data for prediction concerning 'converter' and 'nonconverter' participants from MCI to dementia. The top-performing ML models were i) the gradient boosting

classifier with accuracy of 0.93, F1 of 0.86, and Cohen κ of 0.82, and ii) the RF classifier with an accuracy of 0.92, F1 of 0.79, and Cohen κ of 0.71. The authors, using ML techniques, demonstrated the protective role of CR as anarbitrator of conversion to dementia. Furthermore displaying that the participants with a) extra years of education and b) more outstanding vocabulary scores lived longer, deprived of developing dementia.[38]

Zilcha-Mano et al., in 2018, used ML algorithms to identify predictors for antidepressant medication vs. placebo results in drug trials. 174 participants, with unipolar depression of age 75 and above, were randomly allocated to a pill (citalopram) or placebo. The authors used ML with 'recursive partitioning' algorithm to categorize the most robust arbitrators of placebo vs. medication response. The highest signal finding between medication and placebo in support of drugs was for patients with a lower education level (less than equal to 12 years) who experienced a longer duration of depression since their first incident. On the other hand, for individuals with higher education (more than 12 years), the placebo almost outpaced medication. Despite efforts to categorize characteristics associated with medication–placebo differences in antidepressant trials, few reliable findings have emerged to influence participant selection in drug development settings and differential therapeutics in clinical practice. Limitations in the methodologies used, mainly searching for a single moderator while treating all other variables as noise, may partially explain the failure to generate consistent results. The present study tested whether interactions between pretreatment patient characteristics, rather than a single-variable solution, may better predict who is most likely to benefit from placebo versus medication. The authors, for older patients with unipolar depression, recommended considering individuals' education level and length of their depression in drug trials and also in clinical settings.[39]

IX. Challenges and Opportunities for AI in Psychiatry

AI by itself could not replace human empathy. Therefore, collaborations between ML and psychiatrists can be effective in diagnosis and treatment. AI-based technology might enhance psychiatrist's efficiency and improve patient care, while reducing treatment costs. However, AI-based diagnosis in psychiatry is still not generally used in clinical practices as there are many legal, privacy, and ethical matters that impede its acceptance.

X. Conclusion

AI has the power to amplify clinical productivity due to its propensity to handle a vast amount of data suitable for automation. There exists a significant overlap in symptoms between mental disorders. AI is not going to substitute psychiatrists; instead it can provide psychiatrists with insights that can streamline treatment. AI with the potential to improve the accuracy of diagnosing different mood disorders and can assist psychiatrists in providing proper illness detection and subsequent treatment.

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Global Journal of Medical Research: a
Neurology & Nervous System
Volume 22 Issue 3 Version 1.0 Year 2022
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Therapeutic Approaches to Dysthymia

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Abstract- *Introduction:* Dysthymia is a psychic disorder defined by chronic lowering of mood, with a minimum duration of two years, in which fluctuating moments of the emotional state occur. Unlike the clinical picture of "major depressions", dysthymia has milder manifestations, which occur in a non-episodic manner. Even with milder symptoms, dysthymia ends up having a significant impact on patients lives, since, in the vast majority of cases, the diagnosis is made too late. It is a disease that affects 3 to 6% of the world population, mainly individuals in early adulthood, being twice as common in women than in men. The prognosis of this psychic disorder is associated with the chronicity of the disease and the possible comorbidities resulting from the depressive condition.

Keywords: *treatment; pathophysiology; dysthymia; psychiatric disorders; depression; antidepressant drugs.*

GJMR-A Classification: *DDC Code: FIC LCC Code: PZ7.M1484*

Strictly as per the compliance and regulations of:

Therapeutic Approaches to Dysthymia

Abordagens Terapêuticas Para Distimia

Aproximaciones Terapéuticas A La Distimia

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Resumo- Introdução: o termo "distimia" diz respeito a um transtorno psíquico definido pelo rebaixamento crônico do humor, com duração mínima de dois anos, nos quais ocorrem momentos flutuantes do estado emocional. Diferentemente dos quadros clínicos de “depressões maiores”, a distimia possui manifestações mais leves, que ocorrem de maneira não-episódica. Mesmo com sintomas mais leves, o quadro clínico acaba sendo significadamente impactante na vida dos pacientes, uma vez que, na grande maioria dos casos, o diagnóstico é feito muito tardiamente. É uma doença que acomete de 3 a 6% da população mundial, principalmente indivíduos no início da vida adulta, sendo duas vezes mais comum em mulheres do que em homens. O prognóstico desse transtorno psíquico se associa à cronicidade da doença e às possíveis comorbidades advindas do quadro depressivo.

Objetivo: o objetivo deste trabalho é analisar a literatura coletada a respeito de distimia e as possíveis abordagens terapêuticas para a patologia.

Metodologia: a realização de uma revisão de literatura sistemática, por meio de artigos coletados nas bases de dados PubMed, Lilacs e Scielo, utilizando os descritores “Distimia", “Tratamento Depressão", "Antidepressivos", e seus correspondentes em inglês, considerado artigos do período de 2015 até 2021. Além da utilização do livro Goldman-Cecil Medicina, 25a edição.

Discussão: pode-se utilizar qualquer tipo de antidepressivo para o tratamento do transtorno distímico, mas, dados apontam uma maior eficácia dos fármacos inibidores seletivos da recaptação de serotonina, dos antidepressivos tricíclicos e dos inibidores da monoaminoxidase. Além disso, as psicoterapias que se demonstraram mais eficientes para o tratamento da distimia foram a cognitiva e a comportamental.

Conclusão: o diagnóstico precoce da distimia deve ser realizado cautelosamente, diferenciando-o de transtornos de depressão maior e, uma vez estabelecido, deve-se considerar uma abordagem terapêutica baseada na associação da farmacoterapia e da psicoterapia. Essa terapia associada é a mais eficaz para o controle sintomatológico da doença e para uma melhora na qualidade de vida do paciente.

Palavras-Chave: tratamento; fisiopatologia; distimia; transtornos psiquiátricos; depressão; fármacos antidepressivos.

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Abstract- Introduction: Dysthymia is a psychic disorder defined by chronic lowering of mood, with a minimum duration of two years, in which fluctuating moments of the emotional state occur. Unlike the clinical picture of "major depressions", dysthymia has milder manifestations, which occur in a non-episodic manner. Even with milder symptoms, dysthymia ends up having a significant impact on patients lives, since, in the vast majority of cases, the diagnosis is made too late. It is a disease that affects 3 to 6% of the world population, mainly individuals in early adulthood, being twice as common in women than in men. The prognosis of this psychic disorder is associated with the chronicity of the disease and the possible comorbidities resulting from the depressive condition.

Objective: The objective of this work is to analyze the literature collected about dysthymia and the possible therapeutic approaches for the pathology. *Methodology:* to conduct a systematic literature review, using articles collected in the PubMed, Lilacs and Scielo databases, using the descriptors "Dysthymia", "Treatment Depression", "Antidepressants", and their correspondents in English, considered articles from the period 2015 to 2021. In addition to the use of the book Goldman-Cecil Medicina, 25th edition.

Discussion: Any type of antidepressant can be used for the treatment of dysthymic disorder, but data indicate a greater efficacy of selective serotonin reuptake inhibitors, tricyclic antidepressants and monoamine oxidase inhibitors. In addition, the psychotherapies that proved to be most effective for the treatment of this psychiatric disorder were cognitive and behavioral.

Conclusion: the early diagnosis of dysthymia should be performed cautiously, differentiating it from major depression disorders and, once established, a therapeutic approach based on the association of pharmacotherapy and psychotherapy should be considered. This associated therapy is the most effective for the symptomatological control of the disease and for an improvement in the patient's quality of life.

Keywords: treatment; pathophysiology; dysthymia; psychiatric disorders; depression; antidepressant drugs.

Resumen- Introducción: el término "distimia" hace referencia a un trastorno psíquico definido por el decaimiento crónico del estado de ánimo, con una duración mínima de dos años, donde se presentan momentos fluctuantes del estado emocional. Diferentemente de los cuadros clínicos de “depresiones mayores”, la distimia tiene manifestaciones más leves, que se presentan de manera no episódica. Incluso con síntomas más leves, el cuadro clínico acaba teniendo un impacto importante en la vida de los pacientes, ya que, en la gran mayoría de los casos, el diagnóstico se realiza muy tarde. Es una enfermedad que afecta del 3 al 6% de la

población mundial, principalmente individuos en edad adulta temprana, siendo el doble de común en mujeres que en hombres. El pronóstico de este trastorno psíquico está asociado a la cronicidad de la enfermedad ya las posibles comorbilidades derivadas del cuadro depresivo.

Objetivo: el objetivo de este trabajo es analizar la literatura recopilada sobre la distimia y los posibles abordajes terapéuticos de la patología.

Metodología: revisión sistemática de la literatura, a través de artículos recopilados en las bases de datos PubMed, Lilacs y Scielo, utilizando los descriptores, "Dysthymia", "Depression Treatment", "Antidepressants", y sus correspondientes en inglés, considerados artículos desde 2015 hasta 2021. Además del uso del libro Goldman-Cecil Medicina, 25ª edición.

Discusión: cualquier tipo de antidepresivo puede ser usado para el tratamiento del trastorno distímico, pero los datos apuntan a una mayor eficacia de los fármacos inhibidores selectivos de la recaptación de serotonina, los antidepresivos tricíclicos y los inhibidores de la monoaminooxidasa. Además, las psicoterapias que demostraron ser más eficaces para el tratamiento de la distimia fueron las cognitivas y conductuales.

Conclu-sión: el diagnóstico precoz de la distimia debe realizarse con cautela, diferenciándola de los trastornos depresivos mayores y, una vez establecida, se debe considerar un abordaje terapéutico basado en la asociación de farmacoterapia y psicoterapia. Esta terapia asociada es la más eficaz para el control sintomático de la enfermedad y para una mejora en la calidad de vida del paciente.

Palabras clave: tratamiento; fisiopatología; distimia; desórdenes psiquiátricos; depresión; fármacos antidepresivos.

I. Introdução

A depressão é uma patologia definida como um transtorno afetivo, que possui repercussões mentais, corporais e comportamentais (1). O termo "depressão" foi utilizado pela primeira vez em 1960, a fim de caracterizar um estado de desânimo ou perda de interesse na vida e, atualmente, é designado para descrever sintomas de apatia; irritabilidade; perda de interesse e falta de motivação; tristeza, podendo ou não estar acompanhada de crises de choro; agitação ou retardo psicomotor; alterações no sono; perda ou ganho de apetite; desinteresse sexual; sentimento constante de culpa; pensamentos de morte e possíveis tentativas suicidas; desolação e de redução do comportamento adaptativo do sujeito (2,3,4,5).

Segundo a Classificação Internacional de Doenças, a depressão pode ser diagnosticada a partir da presença de alguns sintomas, manifestados durante um período, com certa frequência e intensidade (4). A síndrome pode ser especificada como um transtorno misto de ansiedade e depressão (CID-10 F41.2); como uma reação depressiva breve, prolongada ou mista de ansiedade e depressão (CID-10 F43); como episódios depressivos leves, moderados, graves com ou sem sintomas psicóticos (CID-10 F32); como transtornos depressivos recorrentes (CID-10 F33); e como distimia (CID-10 F34.1), quando caracterizada como um transtorno de humor persistente (4).

O conceito de distimia é definido por um rebaixamento crônico do humor, com duração de pelo menos 2 anos, que pode ser seguido de momentos flutuantes do estado emocional (7, 8, 9). Esse não se enquadra no critério de "transtorno recorrente" ou de "depressões maiores", uma vez que a intensidade de suas manifestações são mais leves e essas ocorrem de maneira não-episódica (4, 6, 7). A principal característica da patologia é o baixo grau de sintomas que, mesmo sendo menos agressivos, acabam causando um grande impacto da vida dos pacientes, dado que se trata de um quadro crônico negligenciado (7).

Sarcasmo, niilismo, exigência e reclamação excessiva são algumas das principais características de pacientes com transtorno distímico, além de tensão, rigidez e resistência às intervenções terapêuticas (7, 8, 9). É comum que os indivíduos acometidos por distimia aparentem ter um comportamento social estável, mas questiona-se a veracidade dessa estabilidade, dado que autores notaram um alto investimento de energia em atividades laborais e reduzido em relacionamentos interpessoais (7, 8, 9).

A patologia possui etiologia complexa e multifatorial, contando com mecanismos de hereditariedade, predisposição, temperamento, estilos de vida, gênero e estressores biológicos e psicológicos (7). Trata-se de uma doença que acomete de 3 a 6% da população mundial, principalmente indivíduos no início da vida adulta, sendo duas vezes mais comum em mulheres do que em homens (7, 8).

Assim como outros casos de depressão, os pacientes com distimia acabam por procurar auxílio médico muito tempo depois do início dos sintomas e, quando o fazem, apresentam queixas mal definidas, como letargia, fadiga e mal-estar (7). Comumente o paciente e seus familiares confundem o transtorno com o estado cotidiano do sujeito, associando seus sinais e sintomas à experiência habitual do paciente (8). Portanto, o diagnóstico de distimia deve ser realizado cautelosamente, uma vez que os pacientes podem apresentar outras comorbidades, dificultando a percepção clínica de sintomas de distimia e, assim, negligenciando diagnósticos desta patologia psíquica (7).

A fim de realizar o diagnóstico adequado do quadro distímico, utiliza-se o Manual de Diagnóstico e Estatística da Associação Psiquiátrica Americana, em sua 4a edição (DSM-IV), o qual determina os seguintes critérios (9):

1. Humor deprimido na maior parte do dia, por pelo menos dois anos. Em crianças e adolescentes, o

humor pode ser irritável e a duração de pelo menos um ano;
2. Presença enquanto deprimido de dois ou mais dos seguintes sintomas: aumento ou diminuição do apetite, insônia ou hipersonia, baixa energia ou fatiga, baixa auto-estima, diminuição da concentração ou indecisão, desesperança;
3. Durante o período de dois anos (um para crianças e adolescentes) do transtorno, nunca ter ocorrido remissão dos sintomas 1 e 2 por mais de dois meses consecutivos;
4. Durante os primeiros dois anos (um para crianças e adolescentes), não ter ocorrido um Episódio Depressivo Maior, isto é, o quadro atual não ser melhor classificado como Transtorno Depressivo Maior Crônico ou em remissão parcial;
5. Nunca ter ocorrido um Episódio Maníaco, Misto ou Hipomaníaco e nunca ter preenchido os critérios para ciclotimia;
6. O transtorno não ocorre exclusivamente durante o curso de um transtorno psicótico crônico, como Esquizofrenia ou Transtorno Delirante;
7. Os sintomas não ocorrem devido ao efeito fisiológico direto de alguma substância (drogas ou medicações) ou devido diretamente a alguma condição médica geral (hipotireoidismo, por exemplo);
8. Os sintomas causam sofrimento significativo ou prejuízo no funcionamento social, ocupacional ou em outras áreas significativas.

(American Psychiatry Association, 1994)

Uma vez realizado o diagnóstico de distimia, deve-se atentar à sub-divisão do mesmo, sendo a patologia classificada como “precoce”, quando iniciada antes dos 21 anos de idade e “tardia" após isso (9). Não se sabe ao certo qual dos dois tipos de distimia é prevalente, mas dados apontam que o prognóstico da doença está relacionado às possíveis comorbidades associadas ao transtorno psíquico, sendo muito comum a evolução para um episódio de depressão maior ou para um transtorno bipolar do tipo II. Alguns poucos casos podem, inclusive, associar-se a transtornos de bipolaridade tipo I (9). 25% dos pacientes com distimia não atingem uma remissão total dos sintomas, assim, relaciona-se o prognóstico da patologia à cronicidade da doença (9).

II. Objetivo

O objetivo deste trabalho é analisar a literatura coletada sobre a distimia e as possíveis intervenções terapêuticas para o tratamento da patologia. Para isso, visa-se realizar uma profunda discussão sobre depressão, atentando-se à sua fisiopatologia e suas diversas classificações, e, posteriormente, realizar um estudo detalhado a respeito dos fármacos antidepressivos e seus mecanismos de ação, para assim concluir quais tipos de fármacos e terapias são ideias para o tratamento da distimia.

III. Justificativa

Uma vez que a distimia é uma patologia que costuma ser sub-diagnosticada e, ao mesmo tempo, bastante incapacitante social e fisicamente, deve-se aprofundar os estudos sobre o assunto. A doença se desenvolve de forma gradual e, na maioria das vezes, o médico só é procurado quando os sintomas já estão bastante avançados, assim, uma comunidade médica com conhecimento avançado sobre o assunto pode ser apta a realizar um diagnóstico precoce e melhorar o prognóstico do paciente.

A ocorrência de comorbidades ao transtorno distímico e a taxa de pacientes que não conseguem ter remissão total dos sintomas são índices que escancaram a importância da patologia. Portanto o estudo detalhado acerca do diagnóstico e tratamento da distimia é indispensável, assim como o engajamento de psiquiatras e demais médicos em realizar uma análise clínica bem direcionada que vise distinguir exatamente qual tipo de transtorno de humor o paciente apresenta.

IV. Métodos

Revisão de literatura sistemática a partir de artigos coletados nas bases de dados Pub- Med, Lilacs e Scielo, utilizando os descritores “Distimia", “Tratamento Depressão", "Anti-depressivos", “Métodos de Potencialização de Antidepressivos”, e seus correspondentes em inglês, considerado artigos do período de 2015 até 2021. Além da utilização do livro Goldman-Cecil Medicina, 25a edição. A literatura coletada será revisada e posteriormente analisada com o objetivo de promover um maior entendimento sobre a fisiopatologia da distimia e a farmacocinética dos antidepressivos recomendados para essa condição psiquiátrica.

V. Discussão

- Fisiopatologia da depressão

Existem diversas teorias que explicam a fisiopatologia da depressão, mas, baseando-se em estudos mais recentes, a principal teoria para o mecanismo da doença é chamada de “monoaminérgica" (10, 11). O sistema monoaminérgico tem sua origem em núcleos no mesencéfalo e no tronco cerebral, e se propaga pelo córtex e pelo sistema límbico (10, 11). Considerando a anatomia desse sistema, a teoria propõe que a instalação de um quadro depressivo ocorre em função de uma menor produção de aminas biogênicas cerebrais, sendo essas a serotonina, noradrenalina e/ou dopamina (10,11,12).

O estudo que defende essa teoria leva em consideração alguns fatores. O primeiro deles é o fato

da serotonina e da noradrenalina, juntos com a acetilcolina, estarem diretamente relacionadas às áreas corticais e subcorticais do cérebro humano e, assim, possuirem atuação nos mecanismos de regulação do sono, humor, apetite, atividades psicomotoras, entre outros (10,11). Além disso, outro fator significativo foi o resultado de estudos que comprovavam a eficácia de fármacos inibidores da monoaminoxidase (IMAO) em pacientes com sintomas depressivos, dado que, quando eram medicados, seus índices de serotonina e de noradrenalina aumentavam e eram restabelecidos (10,11). Por fim, outros estudos analisaram a reação de pacientes após tratamento com fármacos antidepressivos tricíclicos, que foram responsáveis por indicar que essas pessoas adoecidas tinham, como consequência ao tratamento, suas atividades sinápticas aumentadas exponencialmente (10, 11).

Outra teoria relevante para a fisiopatologia da depressão se baseia na participação do imunológico para o desenvolvimento da patologia (10). Essa defende que os sintomas depressivos ocorrem em função do aumento na produção de citocinas pró-inflamatórias, uma vez que essas podem atuar como neuromoduladores e, assim, intervir nos aspectos neuroquímicos, neuroendócrinos e comportamentais dos transtornos de humor (10, 13). Essa relação entre o sistema imune e o sistema nervoso central ocorre por meio de atividades de neutrófilos e macrófagos; por meio da redução na atividade de células natural killer; e pela resposta de linfócitos a mitógenos (10, 13).

Ao se tratar da distimia, sua fisiopatologia não é totalmente compreendida (18). Associa-se a doença a heranças genéticas, principalmente em casos de transtorno distímico precoce, ou seja, antes dos 21 anos de idade (18).

- Classes dos antidepressivos e seus mecanismos de ação

Inibidores da monoaminoxidase (IMAO): atuam por meio da inibição da enzima monoaminoxidase. Essa enzima é responsável pela eliminação dos neurotransmissores localizados dentro dos neurônios, fazendo com que permaneçam por mais tempo na fenda sináptica (14). A enzima monoaminoxidase possui dois mecanismos de ação, a MAO-A é responsável pelo metabolismo de norepinefrina, serotonina e tiromina; enquanto a MAO-B metaboliza, com mais eficácia, a dopamina (15). Os fármacos inibidores da MAO podem ser irreversíveis e, além disso, alguns conseguem bloquear as duas formas da enzima (15). Sendo assim, como representantes dos antidepressivos IMAO não seletivos e irreversíveis, tem-se: Iproniazida; Isocarboxazida; Tranilcipromina; Fenelzina. Dos seletivos e irreversíveis: Clorgilina. E por fim, dos inibidores reversíveis da MAO-A: Brofaromina; Moclobemida; Toloxatona; Befloxatona (14). Para finalizar, os efeitos colaterais apresentados por essa classe de fármacos, são: hipotensão, cefaleia, sonolência, boca seca, ganho de peso, distúrbios sexuais e até mesmo hepatite, parkinsonismo, anorexia (14,15,16).

Inibidores não-seletivos da recaptação de monoaminas (ADTs): agem de modo que bloqueiam a recaptação de monoaminas, sendo as principais a norepinefrina (NE) e serotonina (5-HT), além da dopamina (DA) em menor proporção (13,14). O exato mecanismo de ação dos fármacos ADTs ainda é desconhecido, mas sabe-se que esses são responsáveis por aumentar a eficácia da transmissão monoaminérgica por meio do aumento da concentração sináptica de serotonina e noradrenalina, que ocorre em função do bloqueio da recaptura dessas monoaminas (13). Dessa forma, ocorre a dessensibilização de receptores b1 adrenérgicos, serotoninérgicos 5-HT2 e 5HT1A, presentes no sistema nervoso central (13). Os principais fármacos representantes dessa classe são: Imipramina, Desipramina, Clomipramina, Amitriptilina, Nortriptilina, Doxepina, Maprotilina (13,16). O bloqueio dos receptores é o fator que desencadeia os efeitos colaterais, que se manifestam de maneiras típicas:

- Anticolinérgicos: boca seca, vista turva, aumento da pressão ocular, retenção urinária, taquicardia, constipação, ganho de peso, confusão e disfunções sexuais;
- Histaminérgicos: sonolência, sedação, fadiga, tontura, náusea, ganho de peso, hipotensão e potencialização de drogas depressoras centrais;
- Alfa-1-adrenérgicos: hipotensão postural, taquicardia reflexa, congestão nasal, cefaléia, disfunção erétil, vertigem e tremores;
- Serotoninérgicos: fadiga, cefaléia, alterações no sono, irritabilidade, ganho de peso, hipotensão e disfunção sexual. (13,16)

Inibidores seletivos da recaptação de serotonina (ISRSs): inibem de forma eficaz e seletiva a recaptação de serotonina, causando uma potencialização da neurotransmissão serotoninérgica (13,16). Os fármacos dessa classe são: Fluoxetina, Paroxetina, Sertralina, Citalopram, Fluvoxamina e Escitalopram. Seus principais efeitos colaterais são: náusea, êmese, dispepsia, dor abdominal, diarréia, perda de apetite, perda ou ganho de peso, ansiedade, agitação, insônia, cefaléia, tremores, sudorese, diminuição de libido, retardo de orgasmo ou anorgasmia (13,16).

Inibidores seletivos da recaptação de 5-HT/NE (ISRSNs): realizam um potente bloqueio seratoninérgico, combinado a um leve efeito de recaptação de noradrenalina (13, 16). Esses fármacos agem de maneira rápida na “downregulation" de receptores beta-adrenérgicos, junto à adenosina monofosfato cíclica (13, 16). As drogas representantes dessa classe são: Venflaxina, Milnaciprano e Duloxetina. Seus principais efeitos colaterais são: náuseas, tonturas, sonolência,

hipertensão, sudorese abundante, tremores, diminuição da libido, anorgasmia, retardo ejaculatório e impotência (13,16).

Inibidores da recaptação de 5-HT e antagonistas alfa-2 (ISRAs): inibem a recaptação de noradrenalina e serotonina, de modo que, a longo prazo, promovem a dessensibilização e diminuição do número de receptores beta-adrenérgicos e 5-HT2 (13). Seus representantes são: Nefazodona e Trazodona. Os efeitos colaterais causados por esses fármacos sao: cefaléia, boca seca, sonolência, náuseas, obstipação intestinal e ataxia; também foram relatados turvação de visão, dispepsia, fraqueza e rash cutâneo (13,16). *Inibidores seletivos da recaptação de noradrenalina (ISRNs):* atuam sobre a atividade seletiva da recaptação de noradrenalina, com atividade antagonista de alfa-2 (13,16). O fármaco representativo dessa classe de antidepressivos é a Reboxetina. Seus principais efeitos colaterais são: taquicardia, impotência, hesitação ou retenção urinária, insônia, sudorese excessiva, constipação intestinal e boca seca (13,16).

Inibidores seletivos da recaptação de dopamina (ISRDs): aumentam a liberação de noradrenalina corpórea e, concomitantemente, inibem "in vitro" a captação neuronal de noradrenalina e dopamina (13,16). A droga pertencente a essa classe é a Bupropiona, que possui como efeitos colaterais: agitação, ansiedade, *rash* cutâneo, diminuição do apetite, boca seca e constipação intestinal (13,16).

Antidepressivo noradrenérgico e especifico serotoninérgico (NaSSA): a ação desses fármacos ocorre por meio do aumento de atividades noradrenérgicas e serotoninérgicas centrais. Possui afinidade com receptores histamínicos e isso explica sua atividade sedativa (13, 16). O fármaco representante é a Mirtazapina e tem como efeitos colaterais a sedação excessiva, ganho de peso (principalmente com o uso em doses baixas), boca seca, edema, constipação intestinal e dispnéia (13, 16).

- A distimia e seu tratamento

Todos os pacientes com depressão devem ser rastreados pensando no diagnóstico de distimia e, para isso, recomenda-se que o adoecido seja bem informado sobre a distinção entre os dois transtornos, atentando-o às principais características: início insidioso, sintomas que crescem e decrescem no período de dois anos, podendo, inclusive, haver breves períodos de humor normal (17). Os adoecidos com o transtorno distímico apresentam sintomas mais subjetivos, distúrbios psicomotores menos dramáticos ou neurovegetativos, incluindo anormalidades de sono, apetite e níveis de energia (18).

O tratamento da distimia pode ser baseado na farmacoterapia isolada; na psicoterapia isolada; ou na combinação de ambas formas terápicas (17,18). A abordagem terapêutica baseada, exclusivamente, na farmacoterapia já se demonstrou eficaz no tratamento da distimia (17). Estudos apontam que pacientes com o transtorno distímico respondem bem a tratamentos com fármacos inibidores seletivos da recaptação de serotonina (ISRSs), antidepressivos tricíclicos (ADTs) e inibidores da monoaminoxidase (7, 18). Nesses casos, o uso dos ISRSs é mais recomendado, dado que a resposta terapêutica é semelhante à dos outros medicamentos, mas esses são melhores tolerados pelo organismo (18).

Foi-se relatado também um sucesso terapêutico com o uso de agentes noradrenérgicos, como a Mirtazapina, Nefazodona, Venlafaxia, Duloxetina e Bupropiona (18). Além disso, um estudo verificou a eficácia terapêutica do uso de antipsicóticos de segunda geração para o tratamento da distimia, mas esses possuem menor tolerabilidade e, consequentemente, causam efeitos colaterais significativos, tais como: sedação, ganho de peso ou anormalidades de dados laboratoriais, como o aumento da prolactina (18). Evidências também indicaram efeitos benéficos do uso de Amissulprida em baixas doses (18).

Uma vez que a distimia possui como uma de suas principais comorbidades a ansiedade, estudou-se também o uso de benzodiazepínicos, a fim de controlar esse sintoma (9). Porém, a melhora da sintomatologia depressiva com o uso de benzodiazepínicos ainda não foi comprovada. Assim, atualmente recomenda-se o uso do antidepressivo tricíclico amitriptilina, ao invés de benzodiazepínicos, para pacientes moderadamente deprimidos com altos níveis de ansiedade associada, uma vez que causam menos risco de abuso e possuem sua eficácia comprovada (9).

Apesar dos dados expostos, Dunner defende em seu artigo "Dysthymia and double depression" que o uso de qualquer antidepressivo é eficaz para o tratamento de distimia, sendo necessária uma análise detalhada de cada paciente, atentando-se aos efeitos colaterais de cada fármaco, às comorbidades do indivíduo e cronicidade da doença (8,9,19).

A duração da farmacoterapia no tratamento de distimia ainda não foi estabelecida, porém, é recorrente que os pacientes necessitem de um tratamento contínuo, por longos períodos. Nesses casos, deve-se considerar as mudanças de antidepressivos e/ou ajustes nas doses dos fármacos, a fim de evitar que os pacientes enfrentem momentos de recaí-das e/ou de perda da eficácia da medicação ao longo do tempo (17).

O uso exclusivo da psicoterapia, para o tratamento da distimia, também pode ser eficaz (17). Estudos defendem que existem diversos tipos de psicoterapias que podem ser utilizadas como ferramenta para o transtorno psíquico, tais como a

psicoterapia cognitivo-comportamental, a psicoterapia interpessoal e a psicodinâmica (17,18). Além disso, o Sistema de Análise Comportamental Cognitiva de Psicoterapia (CBASP) tem se demonstrado eficaz para o tratamento de quadros crônicos de depressão. Esse se baseia em uma técnica estruturada para instruir os pacientes com depressão crônica a lidar com encontros interpessoais problemáticos, tornando-os aptos a usar algoritmos de solução de problemas sociais para lidar com suas dificuldades interpessoais (18). O procedimento é chamado de "análise situacional" e seu foco principal são as interações interpessoais, abordando-as de uma forma mais direta e estruturada, diferentemente do que ocorre na psicoterapia interpessoal e na terapia cognitiva (18). No entanto, estudos apontam dificuldade com o tratamento da psicoterapia exclusiva, alegando que esse é mais eficaz quando combinado com a farmacoterapia (9,17,18,19).

Por fim, a intervenção terapêutica mais aceita atualmente e considerada mais eficaz é a que combina a **farmacoterapia** com a **psicoterapia**, sendo preferencialmente a cognitiva ou comportamental (7,8,17,18,19). A farmacoterapia se demonstra mais eficiente em abordar os sintomas depressivos e, concomitantemente a isso, a psicoterapia pode auxiliar o indivíduo a melhorar a sensação de bem-estar, satisfação e autoestima (8). Dessa forma, o planejamento terapêutico combinado pode ser mais eficaz em promover uma melhor qualidade de vida das pessoas distímicas (8).

A eletroconvulsoterapia (ECT) é um procedimento que se demonstrou eficaz para pacientes com depressão maior que não respondem aos antidepressivos (9). Porém, uma vez que a distimia tem caráter leve, a resposta dos pacientes ao procedimento é bastante improvável, apenas em casos que apresentem comorbidades associadas (9).

VI. Conclusão

A distimia é uma doença crônica que cursa com períodos flutuantes, oscilando entre o humor normal do indivíduo e recaídas depressivas, com duração de pelo menos dois anos. Trata-se de uma patologia bastante incapacitante, que pode demandar um tratamento por toda a vida e, dessa forma, esse deve ser idealizado com cautela.

A fim de propor uma intervenção terapêutica eficaz, deve-se realizar o diagnóstico do transtorno o mais precocemente possível, atentando-se às diferenças entre distimia e depressão maior. Uma vez que o diagnóstico foi estabelecido, o médico deve planejar uma abordagem terapêutica baseada na associação da farmacoterapia e da psicoterapia. A escolha dos medicamentos e do tipo de terapia deve ser realizada considerando as particularidades de cada paciente, mas, por meio dessa abordagem, o indivíduo poderá ter o controle de sua sintomatologia e, ao mesmo tempo, uma melhora na qualidade de vida.

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Global Journal of Medical Research: a
Neurology & Nervous System
Volume 22 Issue 3 Version 1.0 Year 2022
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Physical Neuro-Urological Examinationin Patients with Spinal Cord Injury Revisited

By Wyndaele Jean Jacques & Wyndaele Michel

University Antwerp Belgium

Abstract- *Study design:* Retrospective cohort study

Objectives: To show that combining neuro-urological examinations in the lumbosacral area permit to refine the neurological diagnosis by evaluating ascending and descending spinal cord pathways, sacral reflex arcs and the status of the related muscles.

Setting: University Antwerp Belgium.

Methods: Evaluation of perineal sensation with light digital touch (SENSPER), anal sphincter tone(AST) and voluntary contraction (ASC), anal reflex (ASR), bulbocavernosus reflex (BCR) were done in patients with SCI as part of pre urodynamic testing.

Results: 121 individuals were included, 80 males and 41 females, age 46 ± 16 years old, with different levels and completeness of SCI, determined with ASIA/ISCoS International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI). The examination was done 6.6 ± 12 years post lesion. The findings did not differ between gender or age, except that ASR was more frequently absent in women and ASC diminished with increasing age.

Keywords: *SCI, neuro-urological, physical examination, sensation, reflexes, contraction.*

GJMR-A Classification: *DDC Code: 617.482044 LCC Code: RD594.3*

Strictly as per the compliance and regulations of:

Physical Neuro-Urological Examinationin Patients with Spinal Cord Injury Revisited

Clinical Neuro-Urological Examination in SCI

Wyndaele Jean Jacques [α] & Wyndaele Michel [σ]

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Conclusions: The different components of the physical neuro-urological examination give complementary information on parts of the peripheral innervation and ascending and descending nervous pathways sfrom and towards the lower part of the spinal cord, and on the pelvic floor muscular status. Their combination permits togain detailed information on the nervous structures involved in SCI.

Keywords: SCI, neuro-urological, physical examination, sensation, reflexes, contraction.

Data Archiving and Data Availability: The data are in the patient files. Data from the database are available on request to the corresponding author, blinded for patient name and file number and other information that might consist a breach of confidentiality.

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I. Introduction

Besides inspection and palpation of the genitalia, a physical neurological examination is part of the neuro-urological diagnosis in patients with a suspected or known neuropathy such as a spinal cord injury (SCI). The examination comprises different techniques: sensation of touch of the dermatomes in the perineal area (SENSPER), scoring of the tone of the anal sphincter (AST), voluntary contraction of the anal sphincter/pelvic floor muscles (ASC), anal (ASR)and bulbocavernosus (BCR)reflexes, and the cremaster reflex. The tests are notinvasive, and inform about parts of the afferent and efferent peripheral innervation, the related pathways in the spinal cord, and the pelvic floor muscular status (Table 1)[1].When the reasons for the tests are explained, consent is easily obtained. The assessment of SENSPER includes a test of the patient's compliance and reliability by asking for sensation without touching[2].

We looked at data from such examinations (except cremaster reflex) in a cohort of patients with SCI. Our aim was to show that combining neuro-urological examinations in the lumbosacral area permits to refine the neurological diagnosis by evaluating ascending and descending spinal cord pathways, sacral reflex arcs and the status of the related muscles.

II. Materials and Methods

This is a retrospective study on a consecutive cohort of SCI patients, investigated in a standardised way, when they presented for urodynamic evaluation during a period of 2 years. Patient age and sex, cause of SCI, and their neurological status determined following the ASIA/ISCoS International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) were gathered, with the American Spinal Injury Association Impairment Scale score (AIS)(2).No data were included from patients who did not have a urodynamic investigation. The tests were performed 8 ±12 years after SCI as part of regular follow up (n=77) or as part of an extra evaluation (n=44), e.g. for changed spasticity, increase in AD.

The evaluation of the somatosensory afferent innervation was done in the dermatomes S3-S5 with light

touch, blinded for the patient and with fake touching introduced to check for reliability. The findings were scored as 0= absent, 1= presentin all dermatomes and 2= present in part of the dermatomes or only on one side, for which the details are given. in the results. Then followed four tests with an intrarectal fingertip: the AST was graded by gentle lateral stretching ((0= absent with flaccid muscle and sometimes open anus, 1= weak with little resistance, 2= strong resistance); the ASC was scored as 0= no contraction possible, 1= contraction possible, 2 =strong contraction. Distinction was made with a reflex contraction provoked by the introduction of the finger. The ASR was elicited by making a brisk lateral movement of the fingertip in the anus and was considered positive if the sphincter grabbed the finger (0= absent, 1= present but not strong, 2= strong).Finally, the BCR was elicited with a brisk squeezing of the glans penis/clitoris and the same scoring system was used as for ASR [1].The differentiation between scores 1 and 2was subjective but made by experienced physicians.

Institutional Review Board permission was granted (Edge 001176).

Statistical analysis was done with SPSS28, using Chi-Square (value, df, p value) for categorical, ANOVA for age, and Kappa (k, p value) for comparison of the outcome of two different tests. Statistical significance was set at $p<0.05$.

III. Results

The cohort consists of 121patients,80 males and 41 females, age 47 ± 16 years old. The examination was done 6.6 ± 12 years post SCI.AIS was determined 8 ± 17 days before the test .

There was no significant difference between gender (Chi-Square) for SENSPER (5.55, df 2, p=0.062), AST(1.33, df 2, p=0.514), ASC (3.21, df 2, p= 0.200), BCR (5,05, df 2, p=0.80). The ASR reflex was statistically more absent in women: in 54% (22/41) vs in 41% (33/80) of men (12.18, df 2, p=0.002). No influence of age was found on the neuro-urological physical examinations ANOVA for all (but one) test (SENSPER p=0.218; AST p=0.0.751; ASR p= 0.192; BCR p= 0,485; ASC became weaker with raising age (p=0.002).

The findings of the physical examination in the groups with different spinal cord level and lesion type are presented in table 1, together with the innervation used for the sensation, tone, contraction and reflexes tested.

The outcome of the SENSPER was unreliable in 7 patients not included in the study cohort. When the neuro-urological findings were compared in complete and incomplete lesions, a positive statistical significance(chi-square) was found for SENSPER (65.51,df 2, $p<0.001$). In complete lesions 20/67, 30% had touch sensation; in incomplete lesions SENSPER in all dermatomes or in part of them was present in 49/54 (91%) and absent in 5 (9%). Absence of S4-S5 sensation was found in 5 patients with incomplete lesion (1 cervical, 2 thoracic, 1 thoracolumbar and 1 cauda). Twenty patients had sensation but only in parts of the dermatomes (Table 1 score= 2): S3 present both sides and S4-S5 absent in 12 patients, S3 present at one side with S4-S5 absent in 5 patients, S4-S5 present only one side 2 patients, S5present only one side 1patient.Interpretation of ASC was uncertain because of interfering spasticity in 2 patients examined in the same period, who were not included in the cohort.ASC was possible in 3/67 (4.5%) of the complete lesions and in 40/54 (74 %) of the incomplete lesions.

A comparison between complete and incomplete lesions is given for each test in table 1. To evaluate if the different tests gave similar results Kappa was done . Between ASR and BCR an almost perfect relation was found in complete (k 0.810 $p<0.001$) and a good relation in incomplete (k 0.734 $p<0.001$). Significant similarity ($p<0,05$)was in complete lesions found between SENSPER-ASC and AST- ASR but both with a low k (0.118 and 0.202 respectively). In incomplete, significance in similarity of outcome in AST-ASR and AST-BCR had medium k of 0.294 and 0.261 respectively.

The tests were repeated in 31patients who had not shown changes in their neurological status (determination of AIS was done mean 5 days before the second urodynamics and compared with the one done at the time of the first urodynamics, with an interval of 32±31 weeks). All tests were highly reproducible (Table 3).

IV. Discussion

A neuro-urological physical examination includes testing of motor, sensory, muscular and reflex function in the lower sacral segments(table 1).

In our cohort the relation between AIS and SENSPER was highly positive, as would be expected as sacral sensation is used to help determine AIS. But in a number of complete lesions SENSPER was positive, and in a number with incomplete lesion SENSPER was absent. The reasons may be: unsuspected change in the neurological situation since the last determination of AIS, sensation present in part of the perineal area not examined in the original scoring (especially S3 versus S4-S5), insufficient attention to pitfalls and not introducing fake tests, insufficient cooperation of the patient, and presence of multiple lesions [1-3]. A SCI patient may strongly want to feel without being able to do so. Doubtful outcome of SENSPER was found in some patients examined during the same period who reported sensation while not being touched, but they were not included in this study. Finnerup et al evaluated

sensation evoked by painful or repetitive stimulation below injury level in patients with a clinically complete (AIS A) lesion. Their findings suggest retained sensory communication across the injury in complete SCI, and they suggested the term 'sensory discomplete' (4).

Muscle tone is the continuous and passive-partial contraction of the muscle or the muscle's resistance to passive stretch during the resting phase [5].If the AST is slack (our score 0), it mostly indicates peripheral motor denervation while a normal or strong tone(our score1 and 2) points at decentralization. Previous interventions on the anus or lower bowel must be considered, and an overfilled rectal canal at the time of the examination must be avoided. We found the AST globally not related to the AIS score. We also did not find a relation between AST and ASC, while AST was positively related to ASR(minor significance in complete/mediocre in incomplete) and BCR (mediocre in incomplete lesions), suggesting some role of the lowest spinal reflex activity for the tone of the anal sphincter. A negative relation between AST and ASC has been found in non-neurogenic women with provoked vestibulodynia who combined greater PFM resting stiffness with a decrease in the strength of the pelvic floor muscle contraction[6]. Malouf and Kamm presented the case of a women who had suffered a SCI T12-L1 24 years previously [7]. On rectal examination her anus was closed at rest but gaped after digital examination for several minutes. Palpable voluntary ASC was absent. This sign should be distinguished from the "gaping anus" seen in some patients with faecal incontinence or rectal prolapse, where the AST is permanently diminished, and the sphincter remains always open. In patients with a lesion below L1 (n=17) we found in 4 patients an atonic sphincter which on palpation remained open for a short time. A closed but slack sphincter was present in 1, and AST was normal in 12. The perianal skin sensation to light touch was reduced in the Malouf and Kamm's patient. In our group we did not find a statistical relation between SENSPER and AST, which may suggest that pudendal afferent pathways are only playing a reflex related role in AST.

Voluntary contraction of the anal sphincter and the pelvic floor muscles is normally present if the corticospinal tract is preserved and is a sign that the SCI is motor incomplete. The anal sphincter contraction and anorectal motility was studied by Sun et al in a small sample [8]. They found in patients with incomplete spinal lesions (6 high, 11 low and 3 mixed) a low squeeze pressure of the anal sphincter. In those with T10-L1 lesion in our study tone was present in the anal sphincter in the majority, while ASC was mostly absent. This again indicates the importance of the integrity of the lower spinal cord in the preservation of the anal sphincter tone and the independence of descending spinal cord pathways.

It has been described that healthy men have a stronger anal sphincter pressure compared with women, and findings were similar in cases with chronic constipation[9].It is generally accepted that the condition of muscles diminishes with age, and also in our data such influence was seen. Nielsen and Pedersen found no significant correlation between external sphincter thickness and age on endosonography [10]. When the SCI is motor incomplete, Vasquez et al showed in selected cases that a 6-weekprogram of pelvic floor muscle training (PFMT) may have a beneficial effect on promoting voluntary control of neurogenic detrusor overactivity and may reduce incontinence [11]. This indicates that PFMT can interact more broadlythan only through an increase of the muscle strength.

We have no explanation why in our sample ASR was more absent in women, while no gender differences were found for any of the other tests.

The ASR reflex has afferents in the pudendal nerve, which take synapse in the spinal cord and travel back via the inferior hemorrhoidal nerve to the external anal sphincter [12-14].

The BCR is multisynaptic, mediated mostly by the roots S2–4 , occasionally with synapses as high as L5 [15-16]. The efferent innervation can include S5 [16].Impulses from the glans penis and the frenulum run via the dorsal nerve of the penis/clitoris or perineal nerve, mostly through the dorsal roots andback from the motor neurons and pudendal nerves to the external anal sphincter and bulbocavernosus muscles [17-18].Wang et all showed in suprasacral SCI patients with detrusor overactivity, that 63.0% (58 of 92) had a normal bulbocavernosus reflex (BCR) response (19).

ASR and BCR were in our study statistically significantly related ($p > 0.001$), likely due to the similar innervation involved in both reflexes. But some differences between ASR and BCR were seen and may be caused by a difficulty to elicit, especially the BCR, as seen in healthy individuals [20-21].

The presence of sacral reflexes below the level of injury is key to determining an UMN lesion, absence of sacral reflexes defines a lower motor neuron (LMN) lesion [22].

Extrapolation from the neurological examination to the nature of the neurogenic LUTD is only possible to a certain extent. Wyndaele found a correlation between different levels of SCI, the function of the bladder neck and sphincter, and the ACR and BCR. Higher lesions corresponded more with a reflex lower urinary tract and somatic motor activity, lower lesions more with areflexia. With a lesion between thoracic 10 and lumbar 2 as many reflective as a-reflective dysfunctions were found. Detrusor and striated sphincter reflexia/areflexia corresponded significantly with the presence/absence of bulbocavernosus and anal reflexes. The presence or absence of perineal sensation of light touch has been shown to correspond significantly with the presence or

absence of sensation in the lower urinary tract [23]. In SCI patients with thoracolumbar fractures pinprick sensation in the perineal area was shown to have negative predictive value: absence of pinprick sensation predicted poor bladder recovery [24]. Alexander et al found that subjects with greater preservation of sensation in S3-S5 reported greater ability to initiate and control voiding [25].

For a detailed diagnosis of the LUT function after SCI clinical examination alone is not sufficient [23], as also concluded by Moslavac et al [26].Dartos-cremaster reflex is predictive of some aspects of sexual and bladder neck function in men[27]. It has in our study be done in a few patients only and was thus not included in the results.

Pavese et al could predict urinary continence and complete bladder emptying 1 year after traumatic SCI with the full prediction model relying on lower extremity motor score (LEMS), light-touch sensation in the S3 dermatome of ISNCSI, and SCIM subscale respiration and sphincter management.[28] In patients with ischemic SCI the same model was also useful to predict functional bladder outcome [29].

We conclude that different techniques of lumbosacral physical examination give each a complementary information in the neurological diagnosis after SCI. Our results show that in most tests a different outcome is seen. Only BCR and ASR gave good to perfect similarity in the results. But their outcome can be different as seen in some of our cohort. Combining the tests permit to evaluate ascending and descending spinal cord pathways, sacral reflex arcs and the status of the related muscles.

Limitations of our study are that it is retrospective., the interpretation of the tests is done manually by clinicians and is subjective based on experience. Electrodiagnostic tests and cerebral imaging permit semiobjective and objective measurements which are today not often done outside research.

Statement of Ethics: We certify that all applicable institutional and governmental regulations concerning the ethical use of the data were followed during this research.

Conflicts of Interest: the authors have no conflicts of interest.

Author Contributions:

- Wyndaele Jean Jacques collected the file data, put them in a database, made evaluations and wrote the text.
- Wyndaele Michel contributed to data interpretation and read and corrected the text.

Funding: there was no funding for this study

Acknowledgement: We thank E Roelandt for her help with the statistics.

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Table 1: Results of the Examination in Patients with a Different AIS Score and Lesion Level

Nervous system related to the tests / Spinal cord levels and lesion type	SENSPER Afferent: pudendal S3-S5 through fasciculi gracilis towards brain (ref 1)			AST Afferent: pudendal Efferent: pudendal nerve and suprasegmental nuclei (ref 3)			ASC Efferent: corticospinal tract and pudendal nerve (ref 1)			ASR Afferent pudendal S2-S4 Efferent Inferior hemorrhoidal nerve (ref 10-12)			BCR Afferent L5-S4 pudendal Efferent: deep perineal, inferior hemorrhoidal nerve (ref 14-16)			
	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2	
Complete																Total
C1-C8	13	2	4	2	10	7	18	1	-	6	8	5	8	7	4	19
T1-T9	25	4	1	3	19	8	30	-	-	8	13	9	9	13	8	30
T10-L1	8	-	4	4	5	3	11	1	-	9	3	-	9	3	-	12
L2-S3	-	1	1	-	2	-	1	1	-	-	2	-	-	2	-	2
Conus/cauda	1	1	2	1	2	1	4	0	-	4	-	-	4	-	-	4
total	47	8	12	10	38	19	64	3	-	27	26	14	30	25	12	67
Incomplete																Total
C1-C8	1	21	3	2	15	8	17	7	1	8	13	4	10	10	5	25
T1-T9	2	6	1	2	5	2	9	-	-	5	3	1	5	2	2	9
T10-L1	1	6	2	4	4	1	7	1	1	5	3	1	6	3	-	9
L2-S3	-	6	2	1	7	-	4	4	-	2	4	2	2	5	1	8
Cauda	1	2	-	2	1	-	3	-	-	2	1	-	2	1	-	3
total	5	41	8	11	32	11	40	12	2	22	24	8	25	21	8	54
Global total	52	49	20	21	70	30	104	15	2	49	50	22	55	46	20	121
Chi Square between complete and incomplete	65.51, df 2, p<0.001 More absent in complete			1.42, df 2, p= 0.491 No difference			14.470, df 2, p<0.01 More absent in complete			1.156, df 2, p = 0.561 No difference			0.344, df 2, p= 0.842 No difference			

SENSPER= touch sensation perineal dermatomes S3-S5=0 absent, 1= present,2= present in only parts of area; AST= tone anal sphincter; ASC= voluntary contraction anal sphincter; ASR= anal sphincter reflex; BCR= bulbocavernosus reflex. ASC, ASR and BCR are graded as 0= absent, 1=not strong, 2=strong.For AST :0= absent with flaccid muscle and sometimes open anus, 1= weak with little resistance, 2= strong resistance. Complete = AIS A, incomplete= AIS B-D. - = no patient with this finding.

Table 2: Outcome of the Tests in Groups of at Least 7 Patients with the Same Level of Lesion and Complete or Incomplete Lesion

Level injury	Number patients	SENSPER			AST			ASC			ASR			BCR		
		0	1	2	0	1	2	0	1	2	0	1	2	0	1	2
C5 Complete	3	3	-	-	-	1	2	3	-		1	1	1	1	1	1
C5 Incomplete	4	1	3	-	-	4	-	3	1		2	2	-	2	2	-
D8 Complete	5	5	-	-	-	3	2	5	-		1	2	2	2	2	1
D8 Incomplete	2	-	2	-	-	2	-	2	-		1	1	-	1	1	-
L1 Complete	2	2	-	-	-	2	-	2	-		1	1	-	1	1	-
L1 Incomplete	5	1	2	2	3	2	-	5	-		4	1	-	4	1	-
Cauda Complete	4	1	1	2	1	2	1	4	-		4	-	-	4	-	-
Cauda Incomplete	3	1	2	-	2	1	-	3	-		2	1	-	2	1	-

Table 3: Results of Repeated Testing with an Interval of Mean 32 Weeks in 31 Patients who had Unchanged AIS Scores (%).

Test	No change	Appearance while originally absent	Disappearance while originally present	Total	Missing values
SENSPER	26 (84%)	4	1	31	0
AST	24 (83%)	1	4	29	2
ASC	27 (90%)	3	-	30	1
ASR	16 (59%)	7	4	27	4
BCR	16 (67%)	6	2	24	7

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Global Journal of Medical Research: a
Neurology & Nervous System
Volume 22 Issue 3 Version 1.0 Year 2022
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Distressed: An Assessment of Emotional State of Young Adults during a COVID Wave

By Sehaj Gill & Preetinder Gill

Eastern Michigan University

Abstract- *Purpose:* The COVID-19 pandemic has resulted in a heavy toll on public health. The adverse health outcomes have affected the public physically, mentally and emotionally. Waves during the pandemic have resulted in lockdowns that limited people's ability to interact socially. Due to the novel nature of the disruptions the emotional effects of COVID related lock downs have not been adequately studied. This study assessed the effects of the Jan-Feb 2022 COVID wave related lockdown on young adults aged 18 to 25 in the 11 counties that form the Detroit Metro area in the State of Michigan in the United States of America.

Methods: A survey instrument was developed using well validated Depression Anxiety Stress Scales-21 (DASS-21) along with other questions related to demographics, impact of COVID and methods used for obtaining advice. The survey was electronically shared with the target population in the Detroit Metro area with the help of Centiment, a market research company.

Keywords: *depression, anxiety, stress, pandemic, social impact, modes for seeking advice, covid-19 lockdown.*

GJMR-A Classification: *DDC Code: 614.5 LCC Code: RA644.S17*

Strictly as per the compliance and regulations of:

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Sehaj Gill [α] & Preetinder Gill [σ]

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Results: The data analyses show that the target population in the Detroit Metro area suffered from high levels of depression, anxiety, and stress. This was significantly higher for people who identified their gender as other than male or female. Females also had a higher level of stress than males. It was found the COVID lockdown corelated with higher levels of depression and stress. Further, statistically significant high levels of worry and aggressive behaviors were reported as manifestation of the COVID lockdown. Finally, the target population turned to the internet portals and friends and health professionals at a statistically significant level to seek advice.

Conclusion: The Jan-Feb 2022COVID lockdown had significant impact on the emotional state of young adults in the Detroit Metro area. Also, the study identified common manifestations of distressed emotional state in people aged 18 to 25 years.

Keywords: depression, anxiety, stress, pandemic, social impact, modes for seeking advice, covid-19 lockdown.

I. Introduction

The outbreak of the novel coronavirus, officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a Public Health Emergency of International Concern by the World Health Organisation (WHO) in January 2020.(World Health Organization, 2022; Hotez, 2020; Kenny & Mallon 2021) The disease associated with SARS-CoV-2 is called COVID-19.1 In March 2020, WHO declared COVID-19 a global pandemic. (Cucinotta & Vanelli, 2020) As of June 17, 2022, over 535 million confirmed cases of COVID-19, including over 6 million deaths have been reported.(World Health Organization, 2022) Typical symptoms include fever, cough and tiredness. Other symptoms can include, but are not limited to, loss of taste or smell, headaches, and nausea. (Mayo Foundation, 2022)

Besides the direct health effects, COVID-19 has affected human well-being in many other ways. Several virus variants have resulted in waves that have been typically accompanied with lockdowns. (Fisayo & Tsukagoshi, 2021; Zhang et al, 2021) The lockdowns in particular and the pandemic in general have had a severe impact on the world economy and triggered the largest global economic crisis in more than a century. (World Bank Group, 2022) The median global GDP dropped by 3.9% from 2019 to 2020.(Oum, 2022) Social distancing has been one of the main ways in which communities around the world tried to slow down the spread of the disease. (Qian & Jiang,2020) Disruption of normal social connections along with economic disruptions plausibly have had detrimental and diverse psychological effects on various segments of the public. (Singh & Singh, 2020; Ruben & Wessely, 2020) Little is known about the psychological effects.(Canet-Juricet al, 2020; Schelhorn et al, 2022) Studies have been conducted to assess these effects on pregnant women, people with preexisting mental health conditions, incarcerated individuals, migrant workers, international students, children and young adults. (Fakari & Simbar, 2020; Li & Zhang, 2020; Cloud et al, 2020; Liem et al, 2020; Zhai & Du 2020; Buheji et al 2020; Shanahan et al 2022)More studies are still needed to fully understand the mental and emotional effects of COVID-19 on various segments of the public across all geographical areas. (Cipollettaet al, 2022; Liu et al, 2020; Yildirim et al, 2021) This study addresses the dearth of research in assessing the emotional state of young adults during a COVID-19 wave in the Detroit Metro area.

II. Material and Methods

Detroit residents between the ages of 18 and 25 self-reported their conditions via a survey instrument hosted on Centiment. Co, an online survey platform that

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helps to target specific demographics for researchers. (Centiment, 2022) Data were collected between January 19, 2022, and February 7, 2022. The Detroit Metro area was experiencing a COVID wave during the same time. (State of Michigan, 2022) 522 people from the target population responded to the survey. 412 people completed the survey. There are approximately 600,000 people between the ages of 18 and 25 that reside in the Detroit Metro area. (Detroit Regional Chamber, 2022) 384 samples would be needed to achieve 95% confidence level with a 5% margin of error for statistical analysis. (Australian Bureau of Statistics, 2022)The collected responses are greater than the sample size target.

The survey instrument has 4 sections. The first section covered responder demographics. The second section is adapted from the Depression, Anxiety and Stress Scales (DASS-21). The DASS-21 "is a set of three self-report scales designed to measure the emotional states of depression, anxiety and stress. Each of the three DASS-21 scales contains 7 items, divided into subscales with similar content. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest / involvement, anhedonia and inertia. The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The stress scale is sensitive to levels of chronic non-specific arousal. It assesses difficulty relaxing, nervous arousal, and being easily upset / agitated, irritable / over-reactive and impatient". Scores for depression, anxiety and stress are calculated by summing the scores for the relevant items. (Motor Accident Insurance Commission, Australia, 2016; Lovibond & Lovibond, 1996)DASS-21 responses are summarized as extremely severe, severe, moderate, mild, and normal.

The third section is based on the Pew Research Center's Teen Survey.(Jiang, 2020) The questions in this section cover the usage of electronic devices by the sampled population. The fourth section was derived from C.S. Mott Children's Hospital National Poll on Children's Health. (Freed, n.d.) This survey measures effects of COVID-19 restrictions on teens, who rely on their peer and social connections for emotional support. In total, the survey instrument had 46 multiple choices questions.

Descriptive analysis of the data collected was performed to better understand the demographics of the participants. Descriptive analysis also included breakdown of responses per question. Analysis of variance (ANOVA) was used to explore whether there are any statistically significant differences between various groups. Further, ANOVA was used to investigate the relationships between depression, anxiety, stress, and self-reported impact of COVID-19 on social interactions. Finally, ANOVA was used to investigate how young adults in the Detroit Metro area tried to deal with problems related to their emotional states.

III. Results

49% of the respondents identified as female, 46% identified as male. 54% of the respondents self-reported themselves as white or Caucasian, 35% as black of African American, 9% as Latino or Hispanic, 7% as Asian, 3% as Native American or Alaskan Native and 1% as Native Hawaiian or Pacific Islander. A breakdown of respondent by age is shown in table 1.

Table 1: Breakdown of Respondent by Age in Years

Age	Frequency	Percent
18	82	16%
19	50	10%
20	65	12%
21	88	17%
22	58	11%
23	45	9%
24	58	11%
25	68	13%
Other/Undisclosed	8	2%

In response to DASS-21 portion of the survey, most respondents reported their levels as normal. Specifically, 38.8% reported normal depression levels, 37.4% reported normal anxiety levels and 47.6% reported normal stress levels. On the other hand, 26.9% of respondents reported their depression as extremely severe or severe, 36.2% of respondents reported their anxiety as extremely severe or severe and 18.9% of respondents reported their stress as extremely severe or severe. Additionally, it can be concluded that largest number of people reported higher than normal levels of depression, anxiety, and stress. A complete breakdown of the relevant responses is included in table 2. A Pearson correlation analysis for the three emotional states was performed. The states demonstrate a high degree of correlation. The correlation analysis is shown in table 3. Furthermore, moderate degree of statistically significant correlation, with coefficients between 0.24and 0.39, were found between the levels of emotional states and various detrimental behaviors reported by the

respondents. Results of the associated Pearson correlation analysis are also shown in table 3.

Table 2: Descriptive Analysis for Emotional States

Level	Depression		Anxiety		Stress	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Extremely Severe	57	13.8%	99	24.0%	9	2.2%
Severe	54	13.1%	50	12.1%	69	16.7%
Subtotal	111	26.9%	149	36.2%	78	18.9%
Moderate	102	24.8%	82	19.9%	81	19.7%
Mild	39	9.5%	27	6.6%	57	13.8%
Normal	160	38.8%	154	37.4%	196	47.6%
Grand Total	412					

Table 3: Pearson Correlation Analysis for Emotional States and Detrimental Behaviors

	Depression	Anxiety	Stress	Sleep issues	Worry	Sadness	Changes in appetite	Aggressive behavior	Withdrawing from family
Depression		0.67	0.68	0.30	0.39	0.39	0.24	0.37	0.30
Anxiety	0.67		0.73	0.32	0.35	0.30	0.24	0.36	0.21
Stress	0.68	0.73		0.30	0.38	0.36	0.25	0.39	0.24
Sleep issues	0.30	0.32	0.30		0.40	0.41	0.39	0.31	0.23
Worry	0.39	0.35	0.38	0.40		0.55	0.28	0.24	0.27
Sadness	0.39	0.30	0.36	0.41	0.55		0.38	0.29	0.37
Changes in appetite	0.24	0.24	0.25	0.39	0.28	0.38		0.25	0.34
Aggressive behavior	0.37	0.36	0.39	0.31	0.24	0.29	0.25		0.30
Withdrawing from family	0.30	0.21	0.24	0.23	0.27	0.37	0.34	0.30	

p values < 0.05 in all cases

Over 62% of the respondents reported that the COVID-19 wave that was prevalent during the data collection phase has very negative or somewhat negative impact on their social interactions. A complete breakdown of the responses is included in table 4. Respondents used various modes of communication to interact with their family members, friends or loved ones. Most common modes of communications reported were phone calls, social media, gaming platforms and in-person interactions. A complete breakdown of the responses is included in table 5. During the COVID-19 wave prevalent during the data collection phase 53.6% respondents reported experiencing sleep issues, 56.8% respondents reported experiencing worry, 53.2% respondents reported experiencing sadness, 38.6% respondents reported experiencing changes in appetite, 24.8% respondents reported experiencing aggressive behavior and 32.3% respondents reported withdrawing from family. Further, to seek emotional support 57.8% of respondents looked for information on internet portals, 32% used mobile applications, 37.6% looked for professional help and 68.4% talked to people in the family and/or friends.

Table 4: Responses for the Survey Question "How would You Rate the Impact of the Current/Latest COVID-19 Wave on your Social Interactions?"

	Frequency	Percent
Very Negative	127	30.8%
Somewhat Negative	132	32.0%
Subtotal	259	62.9%
No Impact	114	27.7%
Somewhat Positive	27	6.6%
Very Positive	12	2.9%
Grand Total	412	

Table 5: Descriptive Analysis for Communication Modes with Family Members, Friends or Loved Ones

	Text		Phone Call		Social Media	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Every day or almost every day	18	4%	32	8%	40	10%
A few times a week	44	11%	85	21%	63	15%
A few times a month or less	131	32%	145	35%	116	28%
Never	219	53%	150	36%	193	47%
Total	412					

	Gaming Platforms		In-Person (Indoor and/or Outdoor)	
	Frequency	Percent	Frequency	Percent
Every day or almost every day	113	27%	16	4%
A few times a week	91	22%	107	26%
A few times a month or less	87	21%	127	31%
Never	121	29%	162	39%
Total	412			

ANOVA was performed to assess whether levels of depression, anxiety and stress varied by gender. It was found that the p-values of the F-tests were less than 0.05, hence it can be concluded that there are statistically significant differences between the means from one level of gender to another at the 95.0% confidence level. The multiple range tests showed that the levels varied significantly between the following groups. People who self-reported their gender as other had statistically significant higher levels of depression and anxiety when compared to people who self-reported their gender as male or female. People who self-reported their gender as female or other had statistically significant higher levels of stress when compared to people who self-reported their gender as male. Results of the ANOVA are shown in tables 6, 7, 8. Multiple Ranges tests are shown in tables 9, 10, 11. The results of ANOVA didn't show any statistically significant differences related to respondents' race.

Table 6: ANOVA Table for Anxiety by Gender

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Between groups	30.21	3	10.07	3.95	0.0085
Within groups	1040.42	408	2.55		

Table 7: ANOVA Table for Depression by Gender

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Between groups	20.54	3	6.85	3.28	0.0210
Within groups	851.91	408	2.09		

Table 8: ANOVA Table for Stress by Gender

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Between groups	25.87	3	8.62	5.84	0.0006
Within groups	602.06	408	1.48		

Table 9: Multiple Range Tests for Anxiety by

Contrast	Sig.	Difference	+/- Limits
Female - Male		-0.28	0.32
Female - Other	*	1.22	0.97
Female - Prefer Not to Say		0.63	1.30
Male - Other	*	1.50	0.97
Male - Prefer Not to Say		0.90	1.30
Other - Prefer Not to Say		-0.59	1.59

** denotes a statistically significant difference.*

Table 10: Multiple Range Tests for Depression by Gender

Contrast	Sig.	Difference	+/- Limits
Female - Male		-0.26	0.29
Female - Other	*	1.01	0.88
Female - Prefer Not to Say		0.04	1.18
Male - Other	*	1.27	0.88
Male - Prefer Not to Say		0.30	1.18
Other - Prefer Not to Say		-0.97	1.44

** denotes a statistically significant difference.*

Table 11: Multiple Range Tests for Stress by Gender

Contrast	Sig.	Difference	+/- Limits
Female - Male	*	-0.39	0.24
Female - Other		0.72	0.74
Female - Prefer Not to Say		0.39	0.99
Male - Other	*	1.12	0.74
Male - Prefer Not to Say		0.78	0.99
Other - Prefer Not to Say		-0.33	1.21

ANOVA did not highlight any statistically significant differences between levels of depression, anxiety, stress, and self-reported impact of COVID-19 on social interactions. All p-values were greater than 0.05. Similarly, the analysis did not demonstrate any statistically significant difference in the impact of COVID-19 based on gender or race. Tables 12, 13, 14 show that respondents turned to internet portals and professionals for help with their emotional states at statistically significant levels.

Table 12: Analysis of Variance for Depression - Type III Sums of Squares

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
MAIN EFFECTS					
A:Advice from internet	23.35	1	23.35	11.71	0.0007
B:Help from app	1.01	1	1.01	0.51	0.4775
C:Helpfrm professional	12.61	1	12.61	6.32	0.0123
D:Helpfrmfam_friend	4.92	1	4.92	2.47	0.1169

All F-ratios are based on the residual mean square erro.

Table 13: Analysis of Variance for Anxiety - Type III Sums of Squares

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
MAIN EFFECTS					
A:Advice from internet	48.13	1	48.13	20.62	0.0002
B:Help from app	7.10	1	7.10	3.04	0.0819
C:Helpfrm professional	13.97	1	13.97	5.99	0.0148
D:Helpfrmfam_friend	0.82	1	0.82	0.35	0.5536

All F-ratios are based on the residual mean square error.

Table 14: Analysis of Variance for Stress - Type III Sums of Squares

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
MAIN EFFECTS					
A:Advice from internet	20.64	1	20.64	14.22	0.0002
B:Help from app	0.02	1	0.02	0.01	0.9085
C:Helpfrm professional	4.25	1	4.25	2.93	0.0879
D:Helpfrmfam_friend	0.004	1	0.004	0.00	0.9608

All F-ratios are based on the residual mean square error.

IV. Discussion

The analyses show that emotional states of young adults in the Detroit Metro area were concerning. The emotional states were worse for genders other than male. The COVID-19 wave, and the associated lockdown also seems to have coincided with several detrimental behaviors. The young adults used various modes of communication to keep their social interactions active. They turned to various avenues to seek help for their emotional states.

V. Conclusion

Public health administrators could use the findings of this study to develop effective remedial programs. At individual level, young adults should keep channels of communications open via various modes with loved ones and professionals to help elevate their emotional states. The study is the first of its kind for the Detroit Metro area. Additional studies should be conducted in other geographical areas to develop a comprehensive understanding of the emotional states of young people in general and during pandemic lockdowns in specific. Further longitudinal studies will also help deepen the depth of knowledge. Regardless, of the COVID-19 related lockdown the emotional states of young people in the Detroit Metro area were found to be distressed.

Acknowledgments

The authors acknowledge the support of their family in completing this research study.

Disclosure

The authors report no conflicts of interest in this work.

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Abbreviations: Df: Degrees of Freedom

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Global Journal of Medical Research: a
Neurology & Nervous System
Volume 22 Issue 3 Version 1.0 Year 2022
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

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By Rano Ismailova & Gayrat Kariev

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Keywords: chiari malformation type 1, tonsils ectopia, cerebellar syndrome, brainstem auditory evoked potential (BAEP), somatosensory evoked potentials (SSEP), electroneuromyography (ENMG).

GJMR-A Classification: DDC Code: 616.043 LCC Code: QM691

Strictly as per the compliance and regulations of:

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Abstract- **The scientific work presents the results of a neurophysiological examination of 63 patients with cerebellar symptoms in Chiari malformation of type I according to MRI data. All patients underwent a multimodal protocol including BAEP, SSEP and ENMG examination. Neurophysiological criteria of the cerebellar syndrome in type 1 Chiari malformation have been identified, which in a comparative analysis are the most informative in decision making regarding conservative or surgical treatment.**

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I. Introduction

Neurological disorders in case of anomalies of the craniovertebral junction are extremely diverse and consist of both clinical signs of brainstem compression by lowered cerebellar tonsils and liquorodynamic disorders [1,3,7].

Analysis of the dynamics of neurological disorders does not always provide objective information, and a more informative functional quantitative scale for assessing neurological symptoms, proposed by Egorov et al., 2002 [3] determines the dynamics of neurological disorders in the pre- and postoperative period in Arnold Chiari type I (AK type I). A more objective picture of the functional state of the structures of the craniovertebral transition is provided by a comparison of clinical and neurophysiological research data [6,7,10]

Unfortunately, there is still no single system for assessing the degree of functional deficiency in this pathology. At the same time, the high proportion of subjective neurological disorders makes it difficult to determine the degree of compensation of the disease [4,9,10]. The question - to observe or to operate? - is extremely important in the modern practice of neurologists and neurosurgeons. Modern neurophysiological diagnostic methods make it possible to absolutely accurately objectify the level of pathological disorders and determine the degree of functional involvement of certain anatomical structures. Clinical manifestations of Chiari type I anomaly are described in detail in the literature. Many authors identify from 3 to 6 variants of clinical syndromes [3,4,7,10]. Most often, cerebellar, bulbar, pyramidal and syringomyelia variants are distinguished, and almost all researchers of this pathology point to a high proportion of patients with cerebellar disorders in AK type I [8,10]. Comparative analysis of subjective, objective symptoms in AK type I and neurophysiological data of ASEP, SSEP and ENMG in various AK type I syndromes greatly facilitates the decision on the issue of conservative and surgical tactics, however, a small amount of information about such results in the literature determined the purpose of our study.

The purpose of the study is to determine the dependence of the formation of the cerebellar syndrome on the degree of ectopia of the cerebellar tonsils and to identify significant predictors according to evoked potentials in determining conservative or surgical tactics in patients with this syndrome in Chiari type 1 anomaly.

II. Materials and Methods

We studied 207 patients with AK type I who were treated at the Republican Specialized Scientific-Practical Medical Centre of Neurosurgery from 2015 to 2018, aged 18 to 57 years, the number of men was 82 observations, and women were 125 observations. Among them, 63 patients were identified with neurological disorders characteristic of the cerebellar syndrome in AK type I. All patients were divided into groups depending on the degree of displacement of the cerebellar tonsils below the Chamberlain line. The first group consisted of 17 patients with ectopia of 0-5 mm, the second had 75 patients with ectopia of 5-10 mm, the third was 84 patients with ectopia of 10-15 mm, in the fourth group consisted of 31 patients with the displacement and ectopia was more than 15 mm according to MRI study. The control group consisted of 30 healthy individuals.

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The standard for determining the degree of descent of the cerebellar tonsil in Chiari anomalies was the Chamberlain line, passing from the hard palate to the Opistion (a point located in the centre of the posterior edge of the BSO) [2,8,9]. We considered the displacement of the cerebellar tonsils beyond the Chamberlain line up to 5 mm to be acceptable. In our studies, we used the Chamberlain line to guide the anatomical anomalies of the craniovertebral junction and the degree of cerebellar tonsil ectopia (Fig. 1).

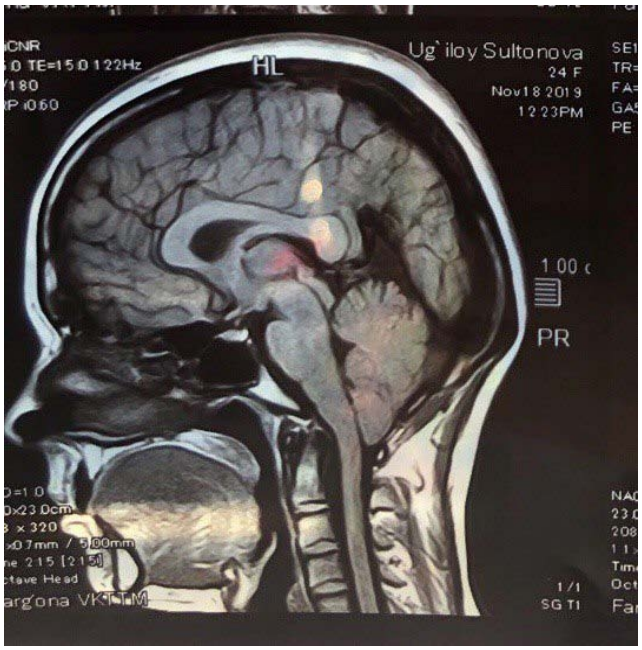

Fig. 1: MRI patient S., 29 years old with an anomaly of the craniovertebral junction with a displacement of the cerebellar tonsils below the Chamberlain line up to 7 mm on both sides with clinical manifestations of cerebellar syndrome.

All patients underwent a multimodal neurophysiological protocol, including acoustic stem evoked potentials (ASEPs), somatosensory evoked potentials (SSEPs), and motor evoked potentials (ENMG) [7]. The studies were carried out on a 4-channel Synapsis complex (Neurotech, Russia) with computer data processing.

For ASEP, the standard vertex-mastoid lead (M1-Cz, M2-Cz) was used.

During SSEP, the electrodes were installed according to the standard C4-Fz method - with stimulation of n.medianus S C3-Fz- with stimulation of n.medianus D. Stimulation was carried out with electrical impulses in the projection of the median nerve at the level of the wrist with a current of 15-20 mA, a frequency of 2 Hz.

Stimulation EMG was performed for n.glossopharyngeus with the establishment of recording electrodes in accordance with muscle innervation. If necessary, we supplemented the studied nerves based on the neurological deficit.

Statistical data analysis was carried out using IBM SPSS Statistics 26 version. Differences in the distribution of quantitative values were assessed using Student's parametric test. To assess the likelihood of surgical treatment, the method of discriminant analysis was used, followed by the construction of a prognostic function, and an assessment of the specificity and sensitivity of the model. Statistically significant differences in the group of operated and non-operated patients were assessed using the Wilks coefficient λ.

III. Results and Discussion

Patients with cerebellar disorders had the highest representation among the examined patients - 63 cases (30.4%).

After analyzing the above complex of subjective and objective neurological symptoms in patients with type I Chiari anomaly, we identified 4 types of clinical syndromes - cerebellar, bulbar, pyramidal, syringomyelitic, which were most clearly formed in groups of patients. The distribution of these syndromes in patients with AK type I, depending on the degree of displacement of the cerebellar tonsils below the Chamberlain line, is proposed in Table 1 (Fig. 2).

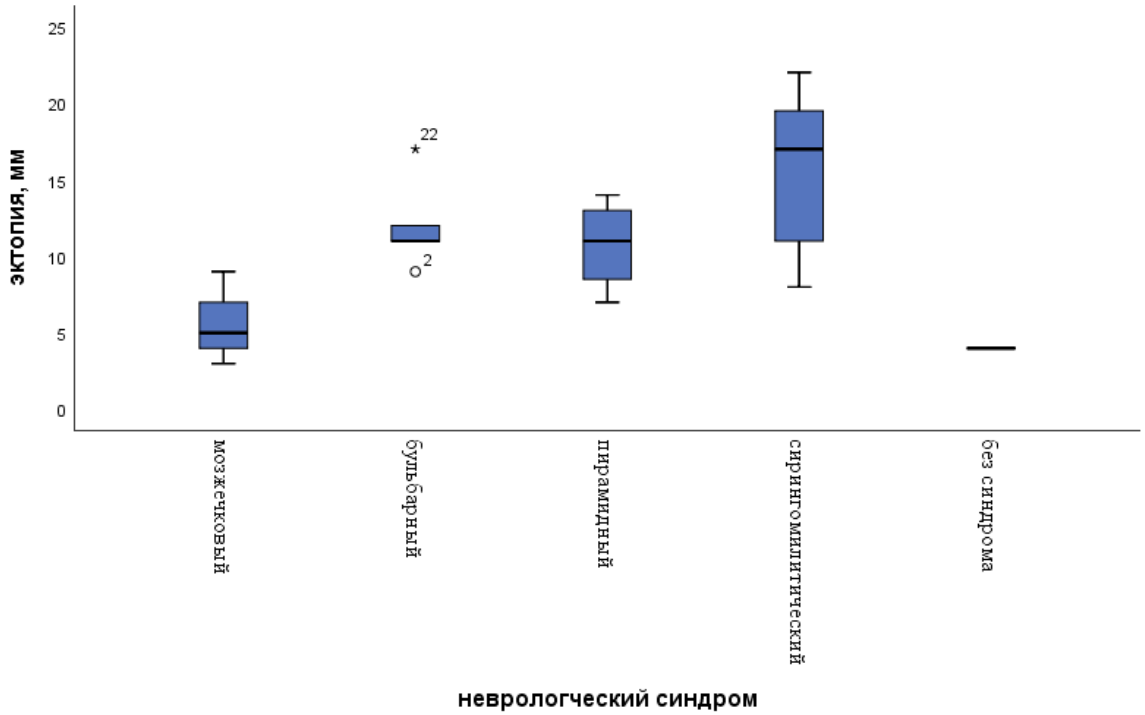

Fig. 2: Structure of neurological syndromes in AK type 1 depending on the degree of cerebellar tonsil ectopia

Table 1: Neurological syndromes in type 1 Chiari anomaly depending on the degree of cerebellar tonsil ectopia

	I group 0-4 mm (n=17)		II group 5-9 mm (n=75)		III group 10-15 mm (n=84)		IV group >15 mm (n=31)	
Syndromes	#	%	#	%	#	%	#	%
Cerebellar	10	58.8	39	52.0	12	14.3	2	6.45
Bulbar	-	-	10	13.3	20	23.8	9	29.0
Pyramidal	-	-	5	6.67	21	25.0	1	3.23
Syringomyelitic	-	-	18	24.0	31	36.9	19	61.3
Without syndromes	7	41.2	3	4.0	-	-	-	-

As can be seen from the presented data, cerebellar syndrome with clinical symptoms of dizziness, tinnitus, various types of nystagmus, static and dynamic ataxia phenomena most often occurred in patients of the I and II groups with tonsil descent to 5-9 mm and accounted for more than half of the cases (58.8% and 52.0% respectively). The representation of cerebellar syndrome in patients of the III and IV groups was significantly less. So, with severe tonsil ectopia of 10-15 mm, the cerebellar syndrome was observed in 12 (14.3%) patients, and in the group with ectopia of more than 15 mm, it was observed in only 2 examined individuals. Such a low number of patients in the III and IV groups with manifestations of the cerebellar syndrome, in our opinion, is associated with the intactness of the cerebellar pathways with a pronounced displacement of the cerebellar tonsils.

Next, we analyzed data from neurophysiological studies in patients with Chiari 1 anomaly.

The data obtained from ASEP studies in patients with cerebellar syndrome are presented in Table 2. It was found that in all examined patients, the latent periods of peaks III and V were extended bilaterally with significant differences compared to healthy individuals. The average values of the latencies of the remaining components - I, II, IV were unchanged compared to the results of the control group. The amplitude indices of the III and V peaks were significantly increased relative to the control values, which dissociated from the general idea of depression of the amplitude indices in ASEP 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 upper olivary complex. An analysis of the average values of the interpeak intervals showed a slight delay in III-V and I-V in the examined group with significant differences with control individuals, which indicated a slowdown in conduction

at the pontomesencephalic level. Peak-to-peak intervals I-III were preserved compared to the control group, which can be explained by the intactness of the peripheral portion of the auditory analyzer.

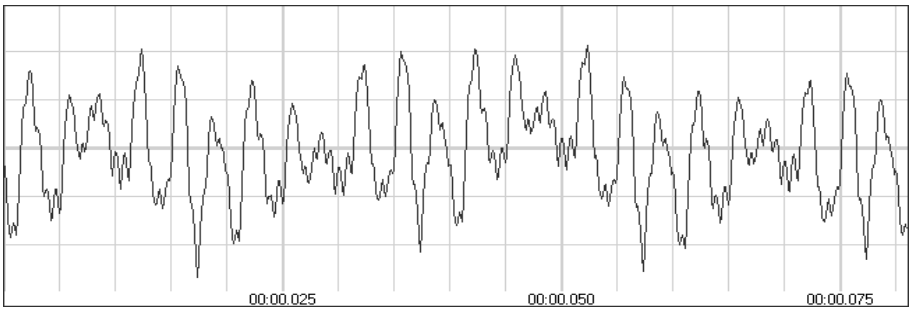

Fig. 3: An example of ASEP in a patient with clinical manifestations of cerebellar syndrome is presented. There is an increase in the amplitude of the PIII peak bilaterally with a relative expansion of the peak-to-peak interval PIII-PV

Table 2: Indicators of acoustic stem EPs - latent period, peak amplitudes and interpeak intervals in healthy individuals of the control group (n=30) and patients with cerebellar AK type I syndrome (n=63)

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=63)					
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=63)			
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*

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=63)			
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 EPs in 63 patients with clinical manifestations of cerebellar AK type I syndrome. Registration of SSEP was performed during stimulation of the median and tibial nerves from 2 sides, the average SSEP values were compared with the values in the control group. The results of the SSEP study in cerebellar syndrome are presented in Table 3.

Table 3: Indicators of somatosensory EPs during median nerve stimulation - latent period, peak amplitudes and interpeak intervals in healthy controls (n=30) and patients with cerebellar AK type I (n=63)

Latency, ms	Control group (n=30)	Cerebellar Syndrome (n=63)
N9 Erb	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 Erb	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
Peak intervals, 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 data, in the group of patients with cerebellar syndrome, there was a significantly significant increase in the latency of the N13 component up to 14.5 ms compared with the control group, which was more often symmetrical bilateral (84% of cases). The amplitude indicators of all SSEP components were preserved relative to healthy individuals. The expansion of the N13-N20 interpeak intervals up to 6.9 ms was isolated in the group of patients with cerebellar AK type I; the parameters of the N9-N13 and N9-N20 interpeak intervals were unchanged compared to the control values.

When analyzing the data on SSEP indicators for stimulation of the tibial nerve, shown in Table 4, 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 study group of patients were not recorded. The N30-P37 peak-to-peak interval was moderately extended to 12.5 ms in the majority of cases (68%) with cerebellar syndrome compared to healthy individuals, the N22-N30, N22-P37 peak-to-peak latencies were consistent with the control group.

Table 4: Indicators of somatosensory EPs during stimulation of the tibial nerve - latent period, peak amplitudes and interpeak intervals in healthy controls (n=30) and patients with cerebellar AK type 1 syndrome (n=63)

Latency, ms	Control group (n=30)	Cerebellar Syndrome (n=63)
N22 lumbar	23.6±1.9	23.2±1.6
N30 cervical	30.6±2.5	38.1±1.2**
P37 Cortex	37.5±3.4	36.±3.0
Amplitude, μV		
N22 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
Peak intervals, 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 SSEP data during stimulation of the median and tibial nerves revealed an increase in the latency of the N13, N30 components in patients with cerebellar AK type 1 syndrome in the predominant number of cases combined with an expansion of the interpeak 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 - the thalamus cortex with a tendency to reduce postsynaptic activation of the nuclei of the medulla oblongata.

We analyzed the ENMG data obtained by stimulation of the oculomotor, facial, glossopharyngeal nerves, as well as the median and tibial nerves in a group of patients with cerebellar disorders in AK type 1. As follows from Table 5 below, motor conduction velocity SPI eff was slightly reduced in the facial and glossopharyngeal nerves with significant differences from the control group. In the oculomotor nerve, the efferent velocity in the study group was preserved relative to the control. The parameters of the conduction velocity of the SPI eff impulse 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 Amax values of the M-response amplitudes for all the studied nerves in the group of patients. However, after stimulation, in 27% of patients with cerebellar syndrome, pathological waves along the facial nerve were noted, while in the group of healthy individuals such a phenomenon was not recorded.

Table 5: ENMG parameters for the oculomotor, facial, glossopharyngeal, median and tibial nerves in healthy controls (n=30) and patients with cerebellar AK1 syndrome (n=63)

Control group (n=30)	SPI eff, 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	-
Glossopharyngeal nerve	42.6±2.0	1860±164.0	-
Median nerve	61.0±1.7	6254±267.0	-
Tibial nerve	49.6±2.1	7125±745.5	-
Cerebellar Syndrome (n=63)			
Oculomotor nerve	29.1±2.0	1072±105.8	
Facial nerve	34.8±1.6**	1130±138.0*	+
Glossopharyngeal nerve	39.2±1.4**	1851±170.5	
Median nerve	60.4±1.5	6158±245.6	
Tibial nerve	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 downward deviations of the SPI eff values in the facial and glossopharyngeal nerves against the background of relatively intact values of the M-response amplitudes indicated the functional involvement of the structures of the pons and medulla oblongata in cerebellar syndrome. Pathological waves along the facial nerve may have corresponded 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 AK type 1 indicated the absence of dysfunction of the segmental apparatus in cerebellar disorders.

Taking into account the above data, we tried to use the discriminant analysis method to identify the likelihood of an operative outcome of treatment in patients with neurological manifestations of the cerebellar syndrome in AK type 1, depending on the degree of tonsil ectopia, as well as quantitative indicators - the amplitudes and latencies of the components of evoked potentials - ASEP, SSEP and ENMG, followed by the construction of a predictive model.

As a result of discriminant analysis by the method of stepwise selection, the following model was obtained (1):

$$Y_{oper}=-8{,}328+0{,}302*X_{ect}+1{,}667*X_{p3\text{-}p5}, \qquad (1)$$

where Y_{oper} is a discriminant function that characterizes the likelihood of surgery in patients with cerebellar syndrome with AK type 1, X_{act} is the degree of tonsil ectopia (mm), $X_{p3\text{-}p5}$ is the latency of the inter-peak interval P3-P5 in ASVP.

The discrimination constant separating patients into operated and non-operated was determined as the value of the function equidistant from the centroids, which amounted to 1.259 in the group of operated patients, and 2.698 in the group of non-operated patients.

The discrimination constant for this model was calculated by the formula - arithmetic mean of centroids (sum/2), or

$$KD=(1{,}259-2{,}698)/2=-0{,}719$$

when comparing the mean values of the discriminant function in both groups of operated and non-operated patients with AK type 1 using the Wilks coefficient λ, statistically significant differences were established (p=0.0001).

Given the calculated values of the prognostic discriminant function, it is possible to determine a high or low probability of the risk of surgical intervention in patients with cerebellar syndrome with Chiari anomaly type 1: with a function value of more than -0.719, the patient belonged to the group with a high probability of surgical intervention, and with a function value of less than -0.719 The risk of surgery was significantly lower.

The sensitivity of the model was 88.2%, the specificity was 100.0%.

Thus, as a result of discriminant analysis, we obtained a function that allows us to predict the likelihood of a surgical outcome of treatment in patients with cerebellar syndrome in AK type 1.

In conclusion, it should be noted that the proposed prognostic model of a conservative or surgical outcome of the disease in patients with AK type 1 has a significant relationship with the degree of cerebellar tonsil ectopia and changes in neurophysiological parameters according to evoked potentials. At the same time, registration of the expansion of interpeak latencies P3 and P5 according to the ASEP study is especially important in addressing the issue of surgical intervention in patients with manifestations of cerebellar syndrome in AK type 1.

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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.

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.

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

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

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

Segment draft and final research paper: You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

Written material: You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

Criterion for Grading a Research Paper (Compilation) by Global Journals

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

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

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ISSN 9755896