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Volume 2 | Issue 2 | December 2020 | Page1-37
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Contents

ARTICLE

1 **Low-intensity Microwave Radiation of Natural Substances for Physiotherapy**
Yanenko O. Peregudov S. Shevchenko K. Grubnik B. Golovchanska O.

11 **Application of Simple Head Cooling Combined with Gangliosides in Neonatal Hypoxic-ischemic Encephalopathy**
Zhen Zhan Huanhuan Cheng Xianhong Lin Yangyang Meng Liying Dai Hong Zheng Qilian Xie

18 **Playing Online Game Increase Aggressive Behaviour of High School Students on 4.0 Century in Papua**
Agussalim M. Natsir Sisilia Teresia Rosmala Dewi Sukatemin Fitria Setiawan Anna Veronica Pont

32 **Deep Learning In Medical Imaging and Drug Design**
Surayya Ado Bala Shri Ojha Kant Adamu Garba

REVIEW

6 **Call to Improve Women's Awareness Regarding Emergency Contraception in Arab Societies**
Hanan Elzeblawy Hassan

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ARTICLE

Low-intensity Microwave Radiation of Natural Substances for Physiotherapy

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ABSTRACT

The mechanisms of influence of physiotherapy procedures in ozokerite-paraffin therapy are considered in this paper. It is shown that microwave electromagnetic radiation formed by heated ozokerite-paraffin mixture is an important component of physiotherapy procedures. Using the experimental setup developed by the authors, the radiative abilities of ozokerite, paraffin and their mixtures in the microwave range were investigated. It was found that in the process of cooling the ozokerite-paraffin mixture, during the procedure, negative microwave fluxes occur, affecting the inflammatory processes in the patient's body. The dependences of the microwave radiation level on the composition of the ozokerite-paraffin mixture are investigated. The results of experimental studies allowed us to evaluate the interaction of electromagnetic radiation of ozokerite-paraffin mixtures with human own electromagnetic radiation and to approach the choice of modes of therapeutic interaction more carefully.

1. Introduction

The most common materials of the organic and mineral origin used in physiotherapeutic treatment are ozokerite, paraffin and healing mood (peloids). These dielectric substances are used in physiotherapy for treatment by the method of thermal impact on the stricken area of the patient's body [1-3]. The most commonly used of them is ozokerite, which belongs to the group of petroleum substances, has the highest heat capacity and heat retention capacity and the lowest thermal conductivity. It consists of ceresin (60-85%), paraffin (3-7%), petroleum oils (5-10%) and a small amount of asphaltenes, bituminous substances, methane, ethylene and some others additional substances [1]. Such composition and physical characteristics determine its therapeutic effects. The therapeutic effects of ozokerite include, first of all, anti-inflammatory action. Beside this, it has mechanisms of chemical - acetylholin-like and aestrogen-like and physical - compression (in 1,5 times more than paraffin) action [3].

Pure paraffin is used in physiotherapy technology less

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commonly. Pure paraffin is a white anhydrous substance, which is also characterized by low thermal conductivity, high heat-retaining ability, but lack of chemical activity and is more plastic.

Usually, for physiotherapy procedures, combinations of these materials (ozokerite-paraffin mixtures) are used. In addition to the thermal action, such mixture has a mechanical effect, since cooling reduces it volume and thus way realize compression effect on the treatment site.

In addition, during these procedures the permeability of the skin increases, this leads to increased protein breakdown. As a consequence, the regeneration processes accelerate due to the effect of "irritation" [4].

There are three main factors which act in the treatment with ozokerite and paraffin on the patient's body both locally and at the level of the whole organism: thermal, mechanical and chemical; they act through the direct influence on the area of the body surface according to specialized literature [1-4].

So, the specified influence during thermal treatment is realized by contact method. At the same time, it is known that when heating any dielectric material (physical body) weak noise electromagnetic signals of a wide frequency spectrum arise. Low-intensity electromagnetic radiation (EMR) of the radio and optical bands are used in various types of therapy: microwave (millimeter), low-level light therapy (LLLT) and others [5-7], for influence on the biologically active points and individual skin areas of patients in order to regulate (change) the condition of the human body. The main frequency range of the medical equipment of the microwave band is in the range of 30-120 GHz, and the wavelength range of optical radiation is 280-760 nm [7-10].

Thus, it should be expected that the overall therapeutic effect will be due to both thermal and microwave factors, and therefore a more in-depth study of the spectral composition and other characteristics of EMR of the materials used in physiotherapy, particularly, in ozokerite-paraffin therapy, is relevant task.

The purpose of this work was to conduct an experimental study of the characteristics of microwave radiation of ozokerite and paraffin, as well as their mixture, which is a concomitant factor in performing appropriate physiotherapy procedures. This factor, as a rule, is not taken into account, but can significantly affect the functional state of the body (see, for example [5,9]). Therefore, it is advisable to determine the level of own EMR of the indicated materials, first of all, in the millimeter wavelength range, to take into account its influence during physiotherapy procedures.

2. Theoretical Information and Basics of the Study

The exchange of thermal energy between the surfaces of the applicator of the ozokerite-paraffin mixture and the patient's skin is performed due to the thermal conductivity process described by the Fourier law

$$P_T = \lambda \operatorname{grad} T \cdot \sigma_0 \quad (1)$$

where λ- coefficient of thermal conductivity of a substance or biotissue; grad$T$- temperature gradient between the ozokerite paraffin applicator and the skin, a σ_0- the square of the applicator surface contacting with the skin.

It is known that any heated physical body emits electromagnetic waves over a wide frequency range. According to Planck's law, the distribution of the density of electromagnetic energy emitting by an element with a single body volume is described by the formula

$$S(f,T) = \beta hf\left[\frac{1}{\exp(hf/kT)-1}+\frac{1}{2}\right] \quad (2)$$

where k=1,38·10^{-23} J/K - Boltzmann constant; h=6,63·10^{-34} J·s - Planck constant; T- body temperature; f- radiation frequency; β - the emissivity of the object coefficient (for a completely black body β =1).

Since the radiation of the millimeter part of the microwave range [7,9,10], in relation to which the ratio is performed $hv \ll kT$, has a significant effect on the state of a living organism, then formula (2) turns into the Nyquist formula

$$s(f,T)=\beta kT \quad (3)$$

Thus, taking into account (3), the radiometric receiver with the analysis band $\triangle f$ is able to capture (measure) the integral power of the EMR

$$P=S(f,T)\ \triangle f=\beta kT\ \triangle f \quad (4)$$

However, the coefficients of the emissivity of the applicator β_A and the bio-tissues β_H differ, and thus, there may be flows of the electromagnetic energy exchange between them, which can be defined as

$$\triangle P=(\beta_H-\beta_A)kT\ \triangle f \quad (5)$$

With respect to the human body, realized flows can be positive (plus-energy) - when the applicator emits more than the skin of the patient, and negative (minus-energy), when on the contrary. These flows may cause additional therapeutic effects. Thus, negative EMR flows are able to attenuate the inflammatory process [11-13], due to rob of excess energy which is intrinsic for inflamation.

It should be noted that the radiative ability of the ozokerite-paraffin applicator β_A is determined by the tangent of the dielectric loss angle tg δ_A and the dielectric permeability ε_A of the temperature-dependent components

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of the mixture of ozokerite and paraffin. Thus, according to [14], with increasing temperature from 35°C to 50°C, the dielectric permeability of paraffin decreases from 2.2 to 1.9. At the same time, tangent of the dielectric loss angle increases from 0.0017 to 0.0040. The same dynamics is observed for ceresin (the main part of ozokerite): its dielectric constant reduce from 2.55 to 2.45 and tangent of the dielectric loss angle increase from 0.0008 to 0.0017. However, decrease of the dielectric permeability of paraffin is sharper, especially near + 50°C. In addition, it's necessary to take into account the frequency dependence of these characteristics, especially for the millimeter range EMR, both for physical materials and for biotissues (see, for example, [15]). Thus, it is necessary to assume that the coefficient of radiative ability of the applicator is a function of two variables $\beta_A(f,T)$, and for the surface of the patient's skin - one variable $\beta_H(T)$ Moreover, their temperature dependences differ. All this significantly complicates the theoretical analysis of the process under study. Thus, the radiative ability coefficient of the applicator in the microwave range is advisable to determine relatively to the skin surface of the patient by formula

$$\beta_A(f,T)=P_A(f,T)/P_H(f) \quad (6)$$

where: P_A, P_H - the integral radiation power, respectively, of the applicator and the surface of the human skin in the operating frequency band of the radiometer receiver.

Considering given the above, as well as the lack of literature data on the presence and level of the microwave component of the indicated materials, which has a significant impact on biological objects, the authors conducted experimental study of the radiative ability of ozokerite-paraffin mixture, taking into account the technological features of the treatment process.

3. Apparatus and Methods of Conducting the Research

The materials most commonly used in physiotherapy - ozokerite from the field of Borislav, Lviv region, Ukraine, producted by OJSC TD Ecomed. To study microwave parameters we used indicated specimens, as well as purified paraffin, from pharmacy packaging with the date of manufacturing January 2019.

The study of microwave parameters of the selected materials, taking into account the observed features of physical bodies during heating, was carried out according to the following method of their heating. The test material was placed in a cylindrical metal container with a base radius of 10 mm (which coincided with the radius of the aperture of the horn receiving antenna) and a height of 12 mm. Initially, the container with tested material was heated in the TC-80M-2 thermostat to the required temperature in the range of 36-50°C, the value of which was automatically controlled to within ± 0.25°C. The heating temperature within these limits was also monitored by an alcohol thermometer. The samples were heated for 30 minutes after reaching the temperature of the experiment. The measurement of electromagnetic microwave radiation power of the indicated samples of materials was carried out by means of an experimental stand, the structural scheme of which is presented in Figure 1.

The experimental stand includes a highly sensitive radiometric system (MS) of the millimeter wavelength range and a heater with automatic temperature maintenance, consisting of: 1 power supply; 2 - thermostat; 3 - attenuator; 4 - microwave signal conversion channels; 5 - measuring device (indicator); 6 - test material in the container; 7 - conical receiving antenna; 8 - metal plate of the thermostat; 9 - temperature control device on the plate of the thermostat 8.

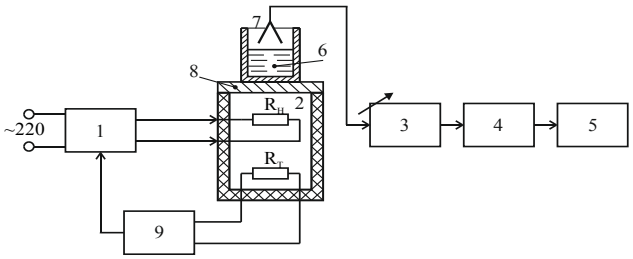

Figure 1. Structural scheme of the experimental studies of the microwave radiative abilities of the ozokerite and paraffin

The temperature on the plate of the thermostat heater 8, using the temperature regulator 9, was pre-set at the test temperature level of the thermostat (TS). Measurement of the temperature of the plate was performed using a contact thermometer of the digital voltmeter B7-27A. During measurements, the receiving antenna was placed directly next to the container.

4. The Results of the Experimental Study

During the study of microwave parameters of the materials were measured and evaluated:

(1) average level of radiation of the skin surface of the person (palms of the hands of two respondents);

(2) changes in the level of radiation during the reuse of ozokerite during the course of treatment with the addition of fresh material;

(3) radiation level of pure ozokerite and paraffin

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at maximum therapeutic temperature of the materials (+50°C);

(4) changes of the power level of EMR of the materials during their cooling;

(5) the power level of EMR of ozokerite depending on the percentage of paraffin impurities;

(6) comparison of the radiation level of materials with the average level of radiation of the human body.

Considering that ozokerite and paraffin are the components of natural oil deposits, the authors additionally carried out measurements of the level of radiation of the oil sample from the Oil field "Shpak Academician" of NJSC "Naftogaz" of Ukraine, which amounted to $2.3 \cdot 10^{-13}$ W.

The average level of radiation power of the human palm surface (limited with antenna aperture area of 2cm^2) of two respondents, measured by RS, was $P_H=(4,5\pm0,5)\cdot10^{-13}$ W in the analysis band frequency of 52±0,1 GHz or, taking into account the aperture area of the measuring antenna, was $2,25\cdot10^{-13}$ W/cm^2.

Typically, the recommended course of treatment is up to 10 procedures with adding of 25% fresh material before each session. Measurements of the selected samples during the treatment cycle did not reveal any significant changes in the parameters of EMR with the addition of fresh portions of ozokerite.

The distribution of the relative radiative power of the ozokerite-paraffin mixture with different percentages of paraffin impurities and the dynamic changes in the level of radiation of the materials during their cooling are presented in Figure 2.

The figure shows that negative flows ($\beta_A/\beta_H<1$) for a typical mixture (ozokerite - 90%, paraffin - 10%) can be realized for a temperature below 45°C. In addition, there is a certain "saturation effect" of the curves in the temperature range of 45-50°C. This can be explained by the peculiarities of the temperature dependences of the tangent of the dielectric loss angle (absorption of EMR) and the dielectric permeability of paraffin and ozokerite (ceresin).

On the one hand, the radiative power of the applicator is proportional to its absorption capacity (Kirchhoff's law) and should increase with increasing temperature. On the other hand, by changing the dielectric permeability, electromagnetic matching between the receiving antenna and the emitting material is disturbed and RS fixes a smaller power value.

The absolute values of the EMR level at the maximum therapeutic temperature of 50°C are shown in Table 1. They can see that the level of radiation of pure ozokerite at the maximum therapeutic temperature of the materials (+50°C) is $5,1\cdot10^{-13}$W (or $\approx 2,55\cdot10^{-13}$W/cm^2) and is comparable with the EMR of the human body.

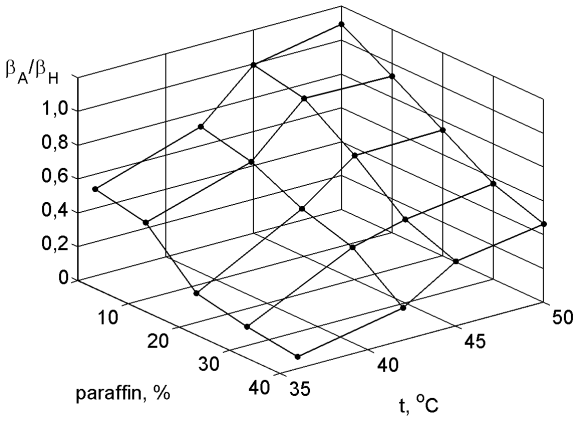

Figure 2. Dependence of relative radiative ability of ozokerite-paraffin mixture on temperature and paraffin content

Table 1. The level of radiation and relative radiation ability for therapeutic temperature +50°C

Material		P,10^{-13}W	$\frac{\beta_A}{\beta_H}$
Mixture (%):			
ozokerite	paraffin		
100	0	5,1	1,10
90	10	4,5	0,90
80	20	2,9	0,78
70	30	2,4	0,59
60	40	1,8	0,45
0	100	0,7	0,15
Oil		2,3	0,51
Human (palm)		4,5	1

The EMR level of pure paraffin at this temperature reaches only $0,71\cdot10^{-13}$W, which is much lower than in humans and can cause forming negative EMR flow. The intensity of such a stream increases with its percentage content grows in a mixture with ozokerite.

5. Conclusions

(1) Thus, as experimental studies show, the materials used in ozokerite-paraffin physiotherapy, form low-intensity electromagnetic radiation, which along with the thermal action affect the body of the patient.

(2) The pure ozokerite applicator at the maximum temperature of +50°C forms a low-intensity positive flow of EMR. Lowering the temperature of the applicator to

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+45°C leads to the formation of a negative flow of EMR, the intensity of which increases with the further cooling of the applicator.

The total power of the ozokerite applicator EMR, for example, 100cm^2 in size, can be $2{,}55 \cdot 10^{-11}$ W, which is comparable to the power used in millimeter therapy [5,7] .

(3) The use of ozokerite-paraffin mixture in the therapeutic temperature range leads to the formation of a negative flow of EMR, which increases as the percentage of paraffin in the mixture grows.

(4) Experimental studies of EMR of the materials for ozokerite-paraffin therapy have shown the complexity of electromagnetic microwave processes that have an effect and interact with the electromagnetic field of the human body and need to be taken into account when conducting physiotherapy.

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REVIEW

Call to Improve Women's Awareness Regarding Emergency Contraception in Arab Societies

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ABSTRACT

Birth spacing means allowing three years or more between two children or two pregnancies. Globally, contraceptive prevalence among married women has increased from 30 percent in the early 1960s to 58 percent in 1998. In ISLAM, the Quran had clearly Indicated the proper time span which should elapse between the birth of one child and the next. The carrying of the child (pregnancy) to Fissal is (weaning) a period of thirty months.

1. Birth spacing OR Family planning

It means allowing three years or more between two children or two pregnancies. You deserve to get the amount of kids you deserve when you want them.

2. In ISLAM

The Quran had clearly Indicated the proper time span which should elapse between the birth of one child and the next. The carrying of the child (pregnancy) to Fissal is (weaning) a period of thirty months.

2.1 Historical Overview & Key Trends in Family Planning

(1) The family planning program started in developing countries in the 1960s.

(2) Over the past 40 years, the acceptance of family planning has been very drastic.

(3) Globally, contraceptive prevalence among married females has increased from 30 percent in the early 1960s to 58 percent in 1998.

(4) In developing countries, this rise was highest, from 9 percent to 55 percent over the same period.

(5) Contraceptives are used in almost all regions of the world by the majority of women who are married or in a marriage in the reproductive age group (15-49 years). Six-

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ty-three percent of these women used some form of contraception globally in 2017. Contraceptive use in Europe, Latin America and the Caribbean, and North America was above 70%, while in Middle and Western Africa it was below 25%.

(6) There is an unmet need for family planning for more than one in ten married or in-union women worldwide; that is, they affirm that they want to avoid or postpone childbearing but do not use any form of contraception to prevent pregnancy. In Africa, there is an unmet need for family planning for as many as one in five women.

(7) Modern contraceptive methods account for much of the worldwide use of contraception. In 2017, more than half (58.0%) of married or in-union women of reproductive age used a modern family planning system internationally, comprising 92.0% of all contraceptive consumers.

(8) In 2017, the proportion of the demand for family planning met by modern contraceptive methods (the proportion of women currently using a modern method among all women who need family planning) among married or in-union women of reproductive age was 78 percent worldwide. In 2017, this proportion was lowest among regions in Africa, at 56 percent, and above 75 percent in all other regions.

(9) The use of modern contraception methods by couples who want to avoid pregnancy remains poor in some nations. In 2017, in 45 countries (including 32 in Africa), less than half of the total demand for family planning was met by modern methods. More than half but less than 75% of the overall demand was fulfilled by the use of new methods in an additional 64 countries.

(10) Total contraceptive prevalence among married or in-union women of reproductive age is expected to increase between 2017 and 2030, mainly in parts of sub-Saharan Africa and Oceania, increasing from 20% to 29% in Western Africa, from 23% to 32% in Middle Africa, from 43% to 56% in Eastern Africa and from 38% to 43% in Melanesia, Micronesia.

(11) Despite the reductions planned for some countries, the unmet need for family planning is estimated to remain above 10 percent worldwide between now and 2030. In Eastern Africa, where unmet needs are projected to fall from 22 percent in 2017 to 16 percent in 2030, and in Polynesia, from 37 percent in 2017 to 31 percent in 2030, the largest declines are expected.

(12) According to the United Nations median projection version, the number of married or in-union women using contraceptives is estimated to increase by 15 million globally, from 778 million in 2017 to 793 million in 2030. In Africa and Southern Asia, the growth in the number of contraceptive users is projected to be particularly rapid. The number of married or in-union women with an unmet need for family planning is expected to marginally decrease globally, from 142 million in 2017 to 139 million in 2030.

(13) Living up to the international community's commitment to achieving equal access to reproductive health by 2030 would entail increased support for family planning, including through successful government policies and programmes. Access to health care facilities and the realisation of reproductive rights for all people will be vital in order to meet the 2030 Sustainable Development Agenda commitment that "no one will be left behind."

2.2 Family Planning Methods

There are several ways to avoid pregnancy if a person wishes to wait to have children or to decide when to have children. These including:

(1) Barrier
(2) Hormonal
(3) Intrauterine Devices (IUDs)
(4) Natural
(5) Permanent

2.3 Goal of the Birth Spacing Program

(1) To improve the health of mother, children & family. This will be achieved by:
(a) Reduction of maternal morbidity & mortality.
(b) Reduction of the infant morbidity & mortality.
(2) To enable women.
(3) Regulate her fertility safely and effectively by conceiving when desired.

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(4) Remain free of disease, disabilities or death associated with reproductive.

(5) Bear & raise healthy children.

2.4 Importance of Birth Spacing Program

(1) Reduction of maternal morbidity rate.

(2) Reduction of child morbidity rate.

(3) Reductions of low birth weight babies.

2.5 Three Key Factors in Family Planning Counseling

(1) Make sure that family planning is not contraindicated.

(2) Present to the couple the various techniques from the medical point of view that you think they can use safely.

(3) Assist couples, together, to select the best appropriate method.

2.6 Factors Affecting Choosing Methods

(1) Personal values.

(2) Ability to use a method correctly.

(3) How the methods will affect sexual enjoyment.

(4) Financial factors.

(5) Status of the couple relationship.

(6) Prior experience.

(7) Future plan.

(8) Safety and Prevention of sexually transmitted diseases.

2.7 Ideal Contraceptive

(1) Safe.

(2) Efficient 100 percent.

(3) Free of side effect.

(4) Obtainable Easley.

(5) Affordable.

(6) Appropriate to the sexual partner & customer.

(7) Free of repercussions for future births.

3. Emergency Contraception (EC)

Why is there a need for emergency contraception?

Every night, about 10 million couples have sexual contact. About 27,000 crack or slip condoms. Even perfect contractors will experience contraceptive failure & do it.

3.1 What is Contraception for Emergencies?

The use of such procedures after unprotected sex to avoid pregnancy is emergency contraception.

(1) Any form of birth control used after intercourse but before implantation (conception)

(2) Intended to be last chance to prevent pregnancy

(3) Not alternative to regular contraception

(4) Not protection from STDs / HIV

(5) It (EC) is a type of backup birth control that can be taken up to a few days after unprotected intercourse, often referred to as "the morning-after pill."

3.2 Unprotected Intercourse Situations

(1) No method used, including coercive sex.

(2) Sex without using a contraceptive

(3) Contraceptive method failure as:

(a) Condom slippage, leakage or breakage.

(b) IUD was partially or totally expelled.

(c) Missed 2 or more birth control pills.

(d) Where 2 or more days late starting pill pack.

(e) Diaphragm or cervical cap slipped.

(f) Missed your regular contraceptive shot.

(g) More than two weeks of a three-month contraceptive injection were skipped.

(h) A one-month contraceptive injection for more than three days was skipped.

(4) Forced to have intercourse or harassed sexually & raped

(5) To minimize the risk of unwanted pregnancies, women need emergency post-coital approaches.

3.3 Possible Mechanism of Action

Depending on when used during cycle, pills may:

(1) EC works by delaying or inhibiting ovulation.

(2) Disrupting follicular development.

(3) ECPs can prevent fertilization by disrupting the sperm movement and its ability to fertilize an egg.

(4) Have effects after ovulation, interfering with the

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maturation of the corpus luteum

(5) ECPs can affect the lining of the uterus so that a fertilized egg cannot implant (implantation interferes)

In brief:

(1) When given PRIOR to ovulation
(a) Inhibits LH surge
(b) Delays or inhibits ovulation
(2) When given AFTER ovulation
(a) Effect on endometrium
(b) Effect on cervical mucous
(c) Ineffective once implantation has occurred
(d) Will not abort an established pregnancy: i.e. post-implantation

3.4 Options for Emergency Contraception

Special contraceptive pill regimens were started as soon as possible, but not more than 72 hours after unprotected intercourse.

[1] *Progestin-only pills (POPs) regimen.*

[2] *Combined oral contraceptives (COCs) regimen (known as Yuzpe Regimen) .*

[3] *Copper IUDs.*

3.4.1 Progestin-only Pills (POPs)

(1) A single pill containing a 1.5 mg dose of a hormone called levonorgestrel (LNG) is the most common method of emergency contraception.

(2) Reduces pregnancy risk by 89 percent

(a) In the 2nd or 3rd week of their period, 100 women have sex without defense.

(b) Without emergency contraceptives, 8 becomes pregnant

(c) 1 will become pregnant with progestin-only ECPs (reduction of 89 percent)

Dose

(1) The first 0.75 mg dose of levonorgestrel should be given as soon as possible, but not later than 5 days (120 hours) after unprotected intercourse. However, it is often most effective when taken 1-3 days (72 hours) after unprotected sex.

(2) Repeat dose: Same amount taken 12 hours after the first dose.

(a) When pills containing 0.75 mg of levonorgestrel are used, 1 pill should be taken for each dose.

(b) When pills containing 0.0375 mg of levonorgestrel are used, 20 pills should be taken for each dose.

(c) When pills containing 0.03 mg of levonorgestrel are used, 25 pills should be taken for each dose.

3.4.2 Combined Oral Contraceptive Pills Regimen (Yuzpe Regimen)

(1) A mixture of combined oral contraceptive pills consists of an earlier form of emergency contraception known as the Yuzpe form.

(2) This solution is less efficient than the LNG-ECP.

(3) It is only recommended if there is no available LNG-ECP.

Reduces the risk of pregnancy by 75%

In the 2nd or 3rd week of their period, if 10 women have sex.

(a) Without emergency contraceptives, 8 becomes pregnant

(b) Using combined ECPs, 2 will become pregnant (75 percent reduction)

Dose

(1) At least 0.1 mg ethinyl estradiol & 0.5 mg levonorgestrel should be included in each dose, which is equivalent to four tablets of the normal low - dose COCs.

(2) After unprotected sex, the first dose must be taken within 72 hours.

(3) Repeat dose: the same amount taken 12 hours after the first dose has been obtained.

(a) When low-dose COCs are used, 4 pills should be taken for each dose.

(b) When high-dose COCs are used, 2 pills should be taken for each dose.

Effectiveness of ECPs

(a) POP regimen is more effective than COC regimen.

(1) POP regimen is more effective than COC regimen.

(b) Progestin-only pills: 85 percent of pregnancies avoided during normal use, 89 percent avoided when properly used.

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(c) Combined pills: 57% of pregnancies avoided in normal use, 76% avoided when correctly used.

(2) The earlier EC pills are taken, the more effective they are.

Side Effects

(1) Nausea & vomiting are the most common side effect.

(2) Less common: headaches, dizziness, fatigue, breast tenderness, irregular bleeding & spotting.

(3) Side effects are more common for COCs regimen than for POPs regimen.

	Levonorgestrel EC	Yuzpe regimen
Nausea	23.1%	50.5%
Vomiting	5.6%	18.8%
Dizziness	11.2%	16.6%
Fatigue	16.9%	28.5%

3.4.3 Copper IUD for Emergency Contraception

(1) Implanted after unprotected intercourse within 5 days (120 hours).

(2) Extremely successful (0.1 percent rate of pregnancy).

(3) Cramping, excessive menstrual bleeding and spotting are side effects.

(4) It can be used as continuous contraception after insertion.

Comparison with other EC

Time	Postinor-2	YUZPE	Copper IUD
0 - 24 hrs	95%	77%	99%
24 - 48 hrs	85%	36%	99%
48 - 72 hrs	58%	31%	99%
72 → 7 days	Up to 5 days	-	99%

Barriers to Effective Use

(1) Lack of access to EHC

(a) Limited access to GP, clinic or ER

(b) Work or travel schedules, Cost

(2) Lack of awareness of EHC

(a) Most women don't know about the method

(b) Think that it can only be "morning after"

(c) Most health care providers do not routinely discuss EC with their clients

(3) Lack of understanding - patients and medical

(a) Not know about EHC, not understand how it works

(b) Moral beliefs (patient, medical)

(c) Fear of adverse effects

(d) Failure to provide EHC in advance of need

Key Messages for Clients

(1) 72-hour time span (but it is easier sooner)

(2) Safe, reliable, and effective

(3) No potential childbearing effect

(4) Mechanism of action (informed choice)

(5) Do not cause abortion

(6) Side effects: vomiting and nausea

(7) Not as successful for periodic use as other contraceptives

(8) Potential bridge to intermittent contraception

(9) ECPs do not safeguard against STDs,

(10) Outlets to access ECPs

(11) Religion (the religious history of the person, not always predictive of EC interest).

(12) ECPs expenses (covered by Medicaid)

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ARTICLE

Application of Simple Head Cooling Combined with Gangliosides in Neonatal Hypoxic-ischemic Encephalopathy

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ABSTRACT

Objective To investigate the effect of simple head cooling combined with ganglioside therapy on neonatal hypoxic-ischemic encephalopathy (HIE) and its clinical efficacy. **Methods** A total of 100 children with HIE admitted in the neonatal ward of our hospital from August 2018 to October 2020 were selected as the research objects, and were divided into control group and observation group according to the random number table method, with 50 cases in each group. The control group was treated with gangliosides, and the observation group was treated with simple head cooling combined with gangliosides. Observe and compare the clinical performance improvement time, the level of relevant hematological examination indexes before and after treatment, and the neonatal behavioral neurological assessment (NBNA), clinical efficacy, and adverse reactions. **Results** The improvement time of convulsions, disturbance of consciousness, pupil changes, hypotonia, and gastrointestinal dysfunction in the observation group was significantly lower than that in the control group (all $P<0.001$). After treatment, the NSE, IL-6, CK, CK-MB of the two groups of children were significantly lower than before treatment, and the serum calcium and NBNA scores were significantly higher than before treatment, and the decrease or increase in the observation group was significantly higher than that of the control Group (all $P<0.001$). The total effective rate of treatment of children in the observation group (82.00%) was higher than that of the control group (62.00%) ($P<0.05$). There were no obvious adverse reactions in both groups. Conclusion The simple head cooling combined with gangliosides in the treatment of HIE can improve the clinical symptoms, blood test index levels, and NBNA scores. The clinical effect is clear and superior to the single use of gangliosides.

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1. Introduction

Neonatal hypoxic-ischemic encephalopathy (HIE) is one of the common results in neonatal brain damage caused by hypoxic-ischemia because of perinatal asphyxia. HIE seriously threatens the health and life of newborns , About 25%-30% of surviving sick newborns are at risk of neurological sequelae, including epilepsy, intellectual disability, cerebral palsy, etc [1]. The pathophysiological changes of HIE are not yet fully understood, leading to lack of breakthrough treatment methods. At present, comprehensive support and symptomatic treatment are still the main components of standard treatment programs. Mild hypothermia therapy has a clear neuroprotective effect, which can reduce the mortality of HIE and the rate of long-term severe disability. It has been regarded as the standard treatment for moderate and severe HIE[2]. In consideration of the safety, complexity and cost of standard hypothermia therapy, we use simple head cooling to achieve the purpose of treatment in clinic. At the same time, drug therapy is also an important part of HIE treatment. Gangliosides can maintain membrane integrity and regulate brain development. They can prevent cell apoptosis and reduce brain damage. They are widely used as auxiliary drugs for HIE in my country. Under treatment [3]. There are not many clinical reports about simple head cooling combined with ganglioside in the treatment of HIE. This study aims to explore the clinical effect of this treatment regimen in the treatment of HIE and its influence on related observation indicators.

2. Information and Methods

2.1 General Information

100 children with HIE admitted in the neonatal ward of our hospital from August 2018 to October 2020 are selected as the research objects, and the random number table method is used to divide them into the control group and the observation group with 50 cases each. The comparison of general data (gender, delivery method, clinical scale, gestational age, birth weight, Apgar score at 5 minutes after birth) between the two groups showed no significant difference (P>0.05) and was comparable. Inclusion criteria: (1) Meet the diagnostic criteria for neonatal hypoxic-ischemic encephalopathy established by the Neonatal Group of the Pediatric Branch of the Chinese Medical Association[4], and determine the clinical scale based on this diagnostic criteria; (2) both Full-term infant and birth weight ≥2500g; (3) Receive treatment within 6 hours of onset of illness; (4) With the informed consent of the child's family member and sign a letter of commitment. Exclusion criteria: (1) Patients with pregnancy complications during pregnancy; (2) Patients with spontaneous bleeding tendency; (3) Patients with complicated and refractory congenital malformations, acute brain-related diseases, congenital infections and other related diseases (4) Those who are contraindicated with this treatment drug; (5) Those who give up treatment. This clinical study followed the Declaration of Helsinki and passed the review of the Medical Ethics Committee of our hospital.

2.2 Method

After admission, the two groups were actively treated with routine treatments, namely three maintenance treatments (maintain good ventilation and ventilation function; maintain sufficient blood perfusion of the whole body and various organs; maintain high normal blood glucose), three symptomatic treatments (control convulsions, Convulsions; reduce intracranial pressure; eliminate brainstem symptoms). The control group was treated with monosialotetrahexose ganglioside sodium (produced by Harbin Medical University Pharmaceutical Co., Ltd., approval number: Zhunzi H20060422, specification: 20mg) on the basis of conventional treatment. The injection was dissolved and diluted with 20ml 5% glucose, injected intravenously with a dosage of 20 mg each time, once a day, for continuous treatment for 14 days; the observation group was given a simple head cooling treatment based on the treatment of the control group, starting within 6 hours of onset, using ice force Apply the cooling patch to the skin of the child's forehead. At the same time, use a gel ice pack to evenly wrap around the child's head. Replace every hour during the operation to ensure that the temperature of the ice pack and cooling patch is at 7-10°C, and monitor the child's anus. Keep the rectal temperature at 33-34℃ , and monitor the vital signs of the child. Continuous treatment for 72 hours, and slowly and naturally rewarming after the treatment.

2.3 Observation Indicators

(1) Collect and compare the general data of the two groups of children; (2) Record and compare the improvement time of related clinical manifestations (convulsions, consciousness disturbance, pupil changes, hypotonia, gastrointestinal dysfunction) of the two groups of children; (3) Compare the blood test index levels of the two groups of children before and after treatment. Before and after treatment, 5ml of radial venous blood was drawn from the two groups of children. All blood samples were placed in blood collection tubes. After centrifugation at 3500r/min, the serum was separated and stored in a freezer at -15°C

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Table 1. Comparison of general information of the two groups of children

Groups	Cases	Gender (male/female)	Delivery method (eutocia/caesarean section)	Clinical grade (moderate/ severe)	Gestational age ($\bar{x}$±s, weeks)	Admission age ($\bar{x}$±s, hours)	Birth weight ($\bar{x}$±s, kg)	Apgar score at 5 minutes after birth ($\bar{x}$±s, points)
control group	50	27/23	24/26	26/24	39.56±1.25	3.61±1.22	3.28±0.25	3.86±0.83
observation group	50	28/22	27/23	25/25	39.76±1.04	3.52±1.37	3.36±0.18	3.84±1.13
x2/t	-	0.040*	0.360*	0.040*	-0.870	0.353	-1.656	0.101
P	-	0.841	0.548	0.841	0.386	0.725	0.101	0.920

Note: * *is the value of* x^2.

for inspection. Enzyme-linked immunosorbent assay (ELISA) detects serum neuron-specific enolase (NSE) and serum interleukin-6 (IL-6) levels. The kits are all made by Kamisu (Provided by Shanghai) Biotechnology Co., Ltd. The operation method is strictly in accordance with the instruction manual. Use a biochemical analyzer to detect serum calcium, creatine kinase (CK) and MB isoenzyme of creatine kinase (CK-MB) levels; (4) Compare the nerve function score of the two groups of children before and after treatment. Before and after treatment, a systematically trained specialist used the 20-item neonatal behavioral neurological assessment (NBNA) developed by Professor Bao Xiulan [5] to conduct behavioral neurological assessment and scores on the two groups of children. , Including 5 parts of behavioral ability, passive muscle tone, active muscle tone, original reflex and general evaluation. There are 20 assessment items, using a 0-2 point scoring system, with a full score of 40 points, and a total score of ≥35 points as neurological Normal function, a total score of less than 35 points is regarded as abnormal neurological function. The lower the score, the more serious the brain injury and the worse the behavioral neurological evaluation. (5) Compare the clinical efficacy of the two groups of children after treatment. An attending and above specialist physician will evaluate the treatment effect of the children. After treatment, related clinical symptoms such as consciousness disturbance, respiratory failure, abnormal muscle tone, seizures, pupil changes, etc. returned to normal, the amplitude integrated EEG was normal, and the blood test indicators returned to normal, it is remarkable. After treatment, the above-mentioned clinical symptoms and related examinations have been significantly improved and have basically returned to normal after treatment, it is effective. After treatment, the above-mentioned clinical symptoms and related examinations are not significantly improved, or even worse than before, it is invalid. Total effective rate = (remarkable number + effective number)/total × 100%. (6) Record the adverse reactions during the treatment of the two groups of children.

2.4 Statistical Processing

Use spss26.0 statistical software for statistical analysis and processing of all data. The measurement data conforming to the normal distribution are expressed by the mean ± standard deviation ($\bar{x}$±s), the comparison within the group adopts the paired design t test, and the comparison between the groups adopts the t test of the mean of two independent samples; the count data is expressed by [n(%)] Indicates that the x^2 test is used. P<0.05 means the difference is statistically significant.

3. Results

3.1 Comparison of the General Data of the Two Groups of Children

There was no statistical difference in the general data of the two groups of children (gender, delivery method, clinical grade, gestational age, birth weight, admission age, Apgar score at 5 minutes after birth) Significance (P>0.05). See Table 1.

3.2 Comparison of the Improvement Time of the Related Clinical Manifestations of the Two Groups of Children

The improvement time of the related clinical manifestations including convulsions, disturbance of consciousness, pupil changes, hypotonia, and gastrointestinal dysfunction in the observation group was lower than that of the control group. Academic significance ($P < 0.001$). See Table 2.

3.3 Comparison of Blood Test Index Levels before and after Treatment between the Two Groups of Children

Before treatment, there was no statistically significant difference between the two groups of children in the NSE, IL-6, serum calcium, CK, and CK-MB index levels (P> 0.05), comparable. After treatment, the levels of NSE, IL-6, CK, and CK-MB of the two groups of children were

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Table 2. Comparison of improvement time of related clinical manifestations between the two groups of children ($\bar{x}$±*s, d*)

Groups	Cases	Convulsions	Disturbance of consciousness	Pupil changes	Hypotonia	Gastrointestinal dysfunction
Control group	50	6.54±2.12	5.46±1.72	3.46±1.66	8.82±1.88	4.66±1.36
Observation group	50	3.70±1.15	3.60±1.44	2.32±0.98	6.34±1.77	3.22±1.18
t	-	8.328	5.865	4.191	6.792	5.638
P	-	0.000	0.000	0.000	0.000	0.000

Table 3. Comparison of blood test index levels before and after treatment in the two groups of children ($\bar{x}$±s)

Groups	Cases	NSE(ug/L)		IL-6(ng/L)		Serum calcium(mmol/L)		CK(U/L)		CK-MB(U/L)	
		before treatment	after treatment	before treatment	after treatment	before treatment	after treatment	before treatment	after treatment	before treatment	after treatment
Control group	50	49.17±6.22	29.75±4.39*	81.36±8.48	46.38±9.05*	1.68±0.22	1.83±0.21*	309.51±36.19	198.33±19.64*	52.83±8.22	33.09±6.49*
Observation group	50	48.78±5.83	19.58±3.75*	80.77±7.94	29.53±8.33*	1.70±0.23	2.04±0.19*	311.59±36.25	165.55±17.79*	53.27±8.49	25.23±4.07*
t	-	0.323	12.453	0.353	9.687	-0.227	-5.113	-0.287	8.744	-0.269	7.266
P	-	0.747	0.000	0.725	0.000	0.821	0.000	0.775	0.000	0.789	0.000

Note: Compared with before treatment, * $P < 0.001$.

Table 4. Comparison of NBNA scores of the two groups of children before and after treatment ($\bar{x}$±s, points)

Groups	Cases	before treatment	after treatment	*t*	*P*
Control group	50	26.31±2.84	33.22±2.97	-79.866	0.000
Observation group	50	25.91±2.88	37.39±3.60	-80.067	0.000
t	-	0.717	-6.333		
P	-	0.475	0.000		

lower than before treatment, and the difference was statistically significant (P<0.001); after treatment, the levels of serum calcium index of the two groups of children were both Higher than before treatment, the differences were statistically significant (P<0.001). After treatment, the levels of NSE, IL-6, CK, and CK-MB in the observation group were significantly lower than those in the control group, and the differences were statistically significant (P<0.001); after treatment, the observation group Serum calcium index levels were significantly higher than those in the control group, and the difference was statistically significant (P<0.001). See Table 3.

3.4 Comparison of NBNA Scores between the Two Groups of Children before and after Treatment

Before treatment, there was no significant difference in NBNA scores between the two groups of children (P>0.05), and they were comparable. After treatment, the NBNA scores of the two groups of children were higher than those before treatment, and the difference was statistically significant (P<0.001). After treatment, the NBNA scores of children in the observation group were higher than those in the control group, and the difference was statistically significant (P<0.001). See Table 4.

3.5 Comparison of Clinical Efficacy between the Two Groups of Children after Treatment

The total effective rate of treatment in the observation group (82.00%) was higher than that of the control group (62.00%), and the difference was statistically significant (P<0.05). See Table 5.

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Table 5. Comparison of the clinical efficacy of the two groups of children

Groups	Cases	Remarkable (n)	Effective (n)	Invalid (n)	Total effective [*n*(%)]
Control group	50	12	20	19	31(62.00)
Observation group	50	18	23	9	41(82.00)
x^2	-				4.960
P	-				0.026

3.6 Adverse Reactions during the Treatment of the Two Groups of Children

No obvious adverse reactions occurred in the two groups of children.

4. Discussion

Neonatal encephalopathy after postpartum related events is one of the main causes of neonatal diseases in the world. Under the condition that there is a causal relationship between neonatal encephalopathy and hypoxic-ischemic brain damage, it is called neonatal hypoxic-ischemic encephalopathy (HIE). Refers to the complex pathophysiological and cellular molecular changes caused by severe hypoxic-ischemic brain damage in the neonatal period. HIE is not a single event, but a continuous process [6]. Existing studies have shown [7] that the pathophysiological reaction process of HIE is mediated by an excitatory oxidation cascade, and the first energy failure that occurs is characterized by the reduction of ATP production and the increase in lactic acid or acidosis. the second energy failure seems to be related to oxidative stress, inflammatory response, excitotoxicity and eventual cell death. The continuous cascade of reactions will further prevent neuronal regeneration or aggravate brain damage, thereby forming a tertiary brain injury . The above cascade can also be summarized into five main events, namely oxidative stress, mitochondrial dysfunction, intracellular calcium ion overload, excitotoxicity and inflammation. After modern basic medicine gradually understood the progress of the brain injury mediated by this cascade reaction at the cellular molecular level and better clarified its basic mechanism, it began to actively study different potential neuroprotective therapies and adjuvant therapies, through intervention in the cascade reaction or an important step to protect the brain tissue. These promising neuroprotective agents have been tested in animal models and preliminary clinical studies of HIE, targeting different stages of injury: early excitotoxicity, oxidative stress and apoptosis, late inflammation, and neuronal and Regeneration of oligodendrocytes, a variety of drug treatments designed, such as mitochondrial membrane stabilizers, neurotrophic factors, etc.[8]. Experimental studies have shown [9] that hypothermia treatment can inhibit key steps in the cascade, including reducing the destructive effects of secondary energy failure on the brain, slowing down oxidative stress, antagonizing the release of excitatory neurotransmitters, and reducing cells Apoptosis and so on. With the emergence of mild hypothermia treatment and its widespread clinical application, the prognosis of moderate HIE has been significantly improved, and early hypothermia treatment within 3 hours after birth has gradually attracted the attention of clinicians [10].

Mild hypothermia treatment is part of the standard treatment plan in developed areas, but it is still an expensive and unacceptable treatment in a resource-limited environment and requires a professional team to implement it. Taking into account the limitations of professional hypothermia treatment, low-cost, easy-to-access and use cooling methods and treatment plans are required in clinical work to ensure its applicability [11]. Studies have shown that [12] gel ice packs can be safely and effectively successfully induced hypothermia. Therefore, we adopted the above-mentioned low-cost and reusable simple head cooling method, which is more acceptable to family members of patients. During treatment no obvious adverse reactions occurred. Sheng et al. [13] evaluated 10 Chinese RCT trials with 987 newborns and concluded that monosialoganglioside adjuvant treatment of HIE can provide additional benefits in improving short-term clinical effects and reducing long-term neurodevelopmental disorders. Exogenous monosialogangliosides can stably bind to nerve cell membranes, leading to changes in membrane function. Its mechanism of action is to promote nerve cell survival, axon growth and synaptic growth, which makes monosialogangliosides in my country is widely used in the clinical adjuvant treatment of HIE and has shown reliable results. At present, the application effect of these two common clinical treatments for HIE is still unclear. We conducted research on this basis.

The serum level of NSE is very low at physiological level, only exists in nerve cells, and is released outside the

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cell when neuron damage occurs, and enters the peripheral blood through the blood-brain barrier. NSE can be used as an early sensitive indicator of nerve cell damage. The severity of HIE is positively correlated and decreases as the disease improves[14]. IL-6 is a multifunctional immune mediator that regulates cellular immunity and inflammatory response. A few minutes after hypoxia and ischemia, the levels of IL-6 and other inflammatory cytokines increase rapidly, by inducing neuronal apoptosis and increasing toxic factors. Nitric oxide levels promote hypoxic-ischemic brain damage[15]. Hypocalcemia is a common disease of HIE. In the reperfusion stage after hypoxic-ischemic injury, rapid calcium influx into cells is ATP-dependent Na^+-K^+ pump failure and cell necrosis secondary to membrane depolarization Or the main cause of apoptosis, the influx of calcium ions into the cells of multiple damaged organs will reduce the serum calcium concentration[16]. When a newborn is asphyxiated, hypoxia and hemodynamic pathological changes can cause hypoxic-ischemic myocardial damage and abnormal levels of myocardial enzyme spectrum[17]. In terms of the above hematological examination indicators, this study shows that after the single use of ganglioside treatment, the levels of related indicators are improved compared to before treatment, which indicates that gangliosides can promote nerve cell regeneration and reduce nerve cell destruction. Nutritional effect may inhibit the inflammatory response after injury, calcium influx into cells and hypoxic-ischemic myocardial damage; and after simple head cooling combined with ganglioside treatment, the improvement effect of related index levels is better than that of using ganglioside alone Better, it indirectly suggests that the combination therapy can repair nerve damage to a greater extent, inhibit cell apoptosis and oxidative stress, and better inhibit the production of active mediators to participate in pathophysiological reactions, thereby reducing IL-6 secretion and reducing calcium ion internal Intracellular overload caused by flow and promote the recovery of myocardial enzyme spectrum level. In terms of NBNA score, in this study, the NBNA score after combined treatment was higher than that of ganglioside alone, which shows that combined treatment may have a more positive effect on nervous system rehabilitation and long-term nervous system development. This is also true in terms of clinical symptom improvement time and therapeutic efficacy. The total clinical effective rate and related clinical symptom improvement time after combined treatment are better than single treatment. This reflects that simple head cooling can exert the effect of hypothermia treatment. This combined treatment It may have a synergistic effect to effectively prevent the further progression of the disease, thereby improving the overall efficacy. The disadvantage is that the study is retrospective, conducted in one center, and the data is limited. Future studies may need to increase the sample size and conduct multi-center cooperation.

5. Conclusion

The current research on the treatment of HIE has shifted from single hypothermia treatment to seeking to improve the prognosis of children by adding adjuvant drug therapy to the treatment of mild hypothermia[18]. This study introduces a Basically similar treatment options for limited conditions. In summary, simple head cooling combined with gangliosides for HIE can significantly improve clinical symptoms, blood test index levels, and NBNA scores. The clinical efficacy is clear and superior to single ganglioside therapy.

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ARTICLE

Playing Online Game Increase Aggressive Behaviour of High School Students on 4.0 Century in Papua

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ABSTRACT

Introduction: Once the enormity of online games took over the attention of many teens and children so that it brought a big change. Aggressive behavior among adolescents especially high school students from year to year is increasing both in number and forms of aggressive behavior that is raised. **Objectives:** This study aims to determine the relationship between playing online games and aggressive behavior of high school students in Jayapura. **Methods:** The research method used was analytical research using *cross sectional* design. Study the relationship between two variables in a situation or group of objects using a simple linear regression statistical test. **Result:** The correlation effect of Length Playing Game Online with aggressively behavior of students in High School logistic test results obtained meaningful results where the value of p = 0, 00 <0.05. This means that there is an influence or relationship between the lengths of playing online games with the aggressive behavior of high school students. These results indicate that there is a positive relationship between the lengths of playing online games with the aggressive behavior of adolescents. This means that the old variable playing online games can be used as a trigger to predict the emergence of aggressive teenage behavior. The higher the length of playing online games, the higher the aggressive behavior of teenagers, conversely the lower the longer playing online games, the lower the aggressive behavior of teenagers.

1. Introduction

The internet is advancement in information & communication technology, which provides opportunities to get access to information quickly, precisely and affordably. Now many people know the internet and even many people can already operate it and use the internet for their interests. The proliferation of internet services, such as *play stations* or *Facebook* and the

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use of mobile phones which were initially only visible in urban areas, can now be found in remote areas too. Plus the *Wi-Fi area* or *hotspot* that makes it easy for anyone to connect to the internet network for free by using a *notebook* or laptop device. In addition, there are also many internet cafes with *online gaming* facilities, e-mail, *chat, browsing* and Facebook and Twitter social networks that can be used at relatively affordable costs [1].

The Ministry of Communication and Information (Communication and Information) through its official website in 2015, it is estimated that more than 100 million of the 250 million Indonesians are active users of smart phones in 2018[2]. The estimate is evidenced by the survey of Indonesian Internet Service Provider Association (APJII) and Technopreneur in 2017, states that as many as 54, 68 %, namely 143.26 million of the total population of Indonesia 262 million people, are Internet users. This figure has increased compared to 2016 as many as 132, 7 million people. Indeed, if viewed from the graph of internet user growth released, from 1998 to 2017, the number of internet users has increased very rapidly, especially in 2016, an increase of 22.5 million internet users compared to 2015 [2] .

The Entertainment Software Association (ESA) survey (2013) found that everyone has at least one Smartphone that can be used to play games. While 32% of gamers are children under the age of 18 and around 10% of adolescents aged 10-18 years play online games on average three times a day with duration of 1 hour or more per day [3].

The latest data released by the *NPD Group* titled mobile gaming (2014) shows that *mobile game* players are those who play on *smartphones, iPod touches or tablets* that play more frequently and in a longer time compared to 2 years ago. The average time spent playing games increased to 57% to more than 2 hours per day in 2014 compared to 1 hour and 20 minutes in 2012 ago. The average amount of playing time at the highest level is in the age range of 6 - 44 years. Children aged 2-12 years spend a proportion of their time playing games than other activities. They spend an average of 2 hours or more to play games. The survey results seem clear that many children are now addicted to playing online games, especially through Android-based smartphones and tablets [4].

Once the enormity of online games took the attention of many teenagers and minors that brought a big change to the type of children's games today. Of course the difference is very clear when considering the children used to play marbles, kites, chess, yo-yo, tops and balls. Then compared to now that is almost all children who are familiar with online games are no longer interested in playing games like this [5].

Online games make players addicted so they do everything as long as they can play them. For example, just attacking some teenagers from Pekan Baru desperate to kill the lives of friends because of his online game chips asked by victims to be sold because the perpetrators need money The same thing is also done by AD and AZ two students from one private vocational high school (SMK) in Pekanbaru have 6 times snatched due to addiction to playing online games. The case shows that they no longer care about what is happening around them. They also cannot control their emotions to get what they want. Some cases occur in parts of the world, *It is likely that this focus will not diminish in the near future, in part because of the enormous media attention garnered when mass killings (The Columbine High School slayings in 1999) are associated with youth who play violent video games (Ferguson, 2007)*. Besides violence Tri Sula elementary students Perwari Hill T Heigh alleged effects of violent games and movies [6].

A study by psychologists Douglas Jewish and Craig Anderson, shows that there is a possibility that online video game violence might have a stronger effect on aggression against adolescents compared to previous media influences [7]. Online gaming is a very interesting game and interactive. Game online have the game figured some of them violent behavior, teens will behave recurring violence because they are playing the media game [8]. Aggressive behavior among adolescents, especially high school students, has increased from year to year, both in number and in the form of aggressive behavior that is raised. BPS in 2015 noted that the number of mass fights between students that occurred in Indonesia increased from 2008 to 108 cases, in 2011 to 210 cases, and 327 cases in 2014.

The phenomenon of adolescent aggressive behavior in the form of physical aggression has occurred a lot, as conveyed by [9]. Cases of student violence such as brawls occurred in South Tangerang City. This time a student brawl took place on Jalan Bhayangkara, right in front of the Alam Sutera Mosque. The number of students who want to fight is 20 people. In the brawl, students who are known to come from Yuppentek 6 Ciledug, injured two local residents who were parking in the street. The two men were stabbed in the thighs and hands; they were named Mawan and Jepri who tried to break up students who were going to fight [10].

In addition, there is also the phenomenon of adolescent aggressive behavior in the form of verbal aggression and anger as conveyed by Alamy in 2016, one teenager was killed and one other injured after being beaten and hacked by seven young men using sharp weapons. The beatings occurred because the two victims

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and their friends had just visited a cafe on Jalan Kenjeran Surabaya. When they returned home, the victim and his friends who were riding motorbikes crossed Jalan Kenjeran, and from the back appeared seven young men riding three motorbikes. Once overtaking the victim, the seven young men suddenly pulled their motorcycle gas. The victim then got off the motorcycle and rebuked the seven young men. Seven members of the young motorcycle gang did not accept and were angry. They quarreled and fought on Jalan Kenjeran. When seized, one of the motorcycle gang members fell and immediately slashed the victim [11].

Jayapura State Vocational School 3 is one of the schools in Jayapura and follows the development of technology. At the time of the initial survey by researchers at SMK Negeri 3 Jayapura, it was found that the school did not have rules that prohibited students from bringing cellphones to school. This is due to various factors, as stated by the student division (Mr. Edi), among others, because many subjects require practice where the practice is usually done until the afternoon so parents can contact the child and also other reasons namely the condition of the area (Jayapura) which it's usually a demo or similar event that makes parents worried and hard to contact if their child does not carry a cell phone.

Based on the description above, it shows that online games are very popular among teenagers today. The rise of online games finally makes teens want to continue to play it. If online game play is played continuously, adolescents will experience addiction to online games and behave aggressively (Dani and Ngesti, 2014). Therefore, the authors are interested in examining whether there is a relationship between playing online games with aggressive behavior in class XI students at SMK Negeri 3 Jayapura City.

1.1 Statement of the Problem

Based on the problem mentioned above we would like to know a relationship playing online games with the aggressive behavior of high school students in Jayapura.

1.2 Research Purposes

The purpose of this study was to determine the relationship of playing online games with aggressive behavior of high class students in Jayapura, Papua.

2. Study Literature

Online Game

(1) Definition

Online games are activities carried out for fun or fun that have rules so that there are winners and some losers. In addition, the game carries the meaning of a contest, physical or mental, according to certain rules, for entertainment, recreation or to win a bet [5].

According to Eddy Liem, Director of Indonesia Gamer (a lover of games in Indonesia), an online game is a game or game that is played online via the internet, can use a PC (personal computer) or regular game consoles such as PS2, X-Box and the like. As for the Wikipedia dictionary, online games are mentioned referring to a type of games that are played through a computer network, generally played on the internet network. Internet games are generally played by many players at the same time in which one each other cannot know. Usually online games are provided as additional services from online service providers or can be accessed directly through a system provided by the company that provides the game [5].

Online Games (*Online Games*) is a kind of computer games that utilize computer network . The network that is usually used is the internet network, like, and always uses the technology that exists today, such as modems and cable connections. Usually the online game is provided as an additional service from service providers online [11].

Online game is a game that is based electronics and visuals. *Online games* are played by utilizing electronic visual media which usually causes radiation to the eyes, so the eyes get tired and are usually accompanied by headaches. *Online games* consist of many types, ranging from simple text-based games to games that use complex graphics and form a virtual world that is occupied by many players at once. In *online games*, there are two main elements, namely *server* and *client.* The *server* administers the game and connects the *client*, while the *client* is the game user who uses the *server's* capabilities. *Online games* can be called a part of social activities because players can interact with each other virtually and often create virtual communities [8].

Based on Grant, JE & Kim, SW, *online game* graphics technology can be divided into:

(A) Two Dimensions (2D), *games* that adopt this technology are average *games* that are lightweight, not burdening the system. But *games* with 2D image quality are not easy to see when compared to 3D *games*, so the average *online game* now adopts 2.5D technology, which is where the characters played are still 2D but the environment has adopted 3D.

(B) Three Dimensions (3D), Three Dimensional type *games* are *games* with good graphics in reality depictions, most *of these games* have camera shifts up to 360 degrees so that we can see the whole world of *games.* But

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the *game* 3D computer asks a fairly high specification in order to see the 3D *game* terse but displayed perfectly [8]..

(2) Types of *online games*

Online games have many types, ranging from simple text-based games to games that use complex graphics and use the visual world occupied by many players at once. The following are the types of *online games* based on the type of game [10].

(A) *Massively Multiplayer Online First-person shooter games* (MMOFPS), This type of online game takes a first-person perspective so as if the player is in the game in the perspective of the characters being played, where each character has a different ability in the level of accuracy, reflexes and others. This game can involve many people and this game usually takes the *setting of* warfare with military weapons. Examples of this type of game include, *Counter Strike, Call of Duty, Point Blank Quake, Blood, and Unreal.*

(B) *Massively Multiplayer Online Real-time strategy games* (MMOORTS), this type of game emphasizes the greatness of the player's strategy. This game has a special feature where the player must set the game strategy. In RTS, the theme of the game is biased in the form of history (e.g. the *Age of Emperies* series), fantasy (e.g. *Warcraft*) and science fiction (e.g. *Star Wars*).

(C) *Massively Multiplayer Online Role-Playing games* (MMORPG), this type of game usually plays the role of fantasy characters and collaborates to knit a story together. RPG usually leads to collaboration rather than competition. Generally in RPGs, the players are joined in one group. Examples of this game genre are *Ragnarok Online, The Lord of the Rings Online: Shadows of Angmar, Final Fantasy, DotA.*

(D) *Cross-platform online play,* Types of games that can be played online with different devices. Currently console game machines (*console games*) *are* starting to develop into computers that are *equipped* with *open source networks* (*open source networks*), such as *dream cast, play station* 2 and *Xbox* which have online functions.

(E) *Massively Multiplayer Online Browser Game*, Games played on browsers such as Mozilla Firefox , Opera or Internet Explorer. A simple *online* game with a single player can be played with the browser via HTML and *HTML scripting* technology (JavaScript, ASP, PHP, and MySQL).

(F) *Simulation games,* this type of game aims to member experience through simulation. There are several types of simulation games, including *life simulation games, construction and management simulation games* and *vehicle simulation*. In *life simulation games,* the player is responsible for a shop or character and fulfills the store's needs like real life, but in the virtual realm. Character has the needs and lives like humans, such as work activities, socializing, eating, shopping and so on. Usually these characters live in a virtual world filled with characters that other players play. An example of the game is Second Life.

(G) *Massively multiplayer online games* (MMOG), Players play in a large scale world (> 100 players), where each player can interact directly like the real world. MMOG emerged along with the development of *broadband* internet *access* in developed countries, thus allowing hundreds, even thousands of players to play together.

(3) Impact of Playing *Online Games* on Teenagers.

Besides having a positive impact *online games* also have a negative impact. The positive impact in playing this online game is the impact that can be said to give benefits /influence both for its users. Positive impact *online games* can be as follows [12]:

(A) Can master the computer.

(B) By playing *online games* directly, you can understand the English language used in the game which is not uncommon for players to interpret their own words that they don't know.

(C) From this online game you can add friends.

(D) For those who already have an ID from one of their ready-made *online games* (GG) they can sell it to others and eventually get money from the proceeds.

Meanwhile the negative impact of playing *online games* is the unfavorable impact for online game users such as:

(A) Someone who plays *online games* is a waste of time and money.

(B) Playing *online games* makes people addicted.

(C) Sometimes more willing to give up school to play *online games* (skip school).

(D) By playing *online games* can also make sure of the time, to eat, pray, time to go home, etc.

(E) Too often dealing with monitors in the naked eye can make the eyes become a minus.

(F) A child is often lying to his parents because at the beginning he said goodbye to go to school it turns out he skipped school to play *online games*.

Margaretha Soleman put forward the social, physical adverse effects of addiction to playing *online games*, as follows:

(1) Social, relationships with friends and family become tenuous because their time together becomes far less. Adolescent association is only limited to internet *online games*, so that makes online game addicts become isolated from friends and real social environment. Social skills are diminished, making it increasingly difficult to connect with others. Gamers' behavior becomes rude and

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aggressive because it is influenced by what is seen and played in internet games *online games*.

(2) Psychic, teenage mind becomes constantly thinking about the game being played, difficulty concentrating on study, work, often skipping, or avoiding work. Make teens become indifferent, indifferent, less concerned about things happening in the surrounding environment. Do anything to play games, such as lying, stealing money, etc. Being accustomed to only interacting one-way with computers makes teens become closed, it is difficult to express themselves when in a real environment.

(3) Physical, exposure to light from computer radiation can damage the nerves of the eye and brain. Heart health decreases due to not sleeping all night playing internet games online. Kidney and stomach are also affected due to a lot of sitting, drinking less, forgetting to eat because of the fun of playing. The negative impact of the other, namely body weight decreased due to forgetting to eat, or it could also increase because a lot of eating snacks and rarely exercise. Easily tired when doing physical activity, body health decreases due to lack of exercise. The most severe is that it can cause death [13].

3. Method of Research

The research method used in this study is a quantitative method. Quantitative method is a research method that uses statistics in the form of numbers ranging from collecting data, interpreting data, displaying the results, to drawing conclusions from the study. (Lubis 2018). This type of research uses analytic methods with cross sectional research design. This research was conducted at the State Vocational School 3 Jayapura in March to April 2019.

Populations in this study are teenagers of online game players aged 16-17 years old at Vocational School 3 Jayapura. The sample of this study was taken using the consecutive sampling method, where all subjects who came and met the selection criteria were included in the study until the number of subjects needed was fulfilled.

(1) Inclusion criteria; (a) Teenagers aged 16-17 years, (b)online game players.

(2) Exclusion Criteria; (a) Adolescents who refuse to take part in research, (b) Teenagers with a family history of mental disorders.

The data collection is done by way of distributing questionnaires to a sample which would be the respondent and signed *informed consent.* The questionnaire is used to see the level of online game play and for aggressive behavior. Researchers conducted themselves in conducting data collection by first asking for permission from the school.

Data will be analyzed by entering data from the questionnaire into a computer program using the SPSS program. After the data is processed then the data is analyzed descriptively and analytically. Characteristics of respondents and categorical scale data descriptions are described in the form of frequency and percent distribution in the form of tables and analysis of the relationship between variables is done by bivariate analysis using a simple regression hypothesis test.

4. Result of Study

4.1 General Description of Research Location

State Vocational School 3 Jayapura is one of the oldest Vocational Schools among a series of Vocational Schools in Jayapura and even throughout the Land of Papua. The address of SMK Negeri 3 is on the Abepura highway, Kota Raja, RT 002 RW 007 Wahno Village, Abepura District, Jayapura City, and Papua Province. Telephone number 0967-581289, ZIP code 99225, fax 0967-581781, school area of 30,000 m^2. The total number of students is 1,651 students consisting of 706 students of class X, 527 students of class XI and 418 students of class XII. State Vocational School 3 Jayapura has 10 Department / Program expertise, with 14 Skill Competencies, namely:

(1) Study Program Building Skills: (a) Stone & concrete Construction Engineering Skills Competencies, (b) Wood Construction Engineering Skills Competencies, Mechanical Image Building.

(2) Electronics Studies Expertise Program.

(3) Electricity Utilization Study Skills Program.

(4) Mechanical Studies Skills Program; (a) Machining Engineering Skills Competencies, (b) Welding Engineering Skills Competencies.

(5) Automotive Study Skills Program; (a) Light Vehicle Engineering Expertise Competencies, (b) Motorcycle Engineering Expertise Competencies.

(6) Mining Geology Study Skills Program.

(7) Survey Study and Mapping Study Skills Program.

(8) Plumbing and Sanitation Study Skills Program

(9) Computer and Information Studies Skills Program, Computer & Network Engineering Skills Competencies.

(10) Renewable Energy Study Skills Program

4.2 Characteristics of Respondents

(1) Age

Table 1. Distribution of Respondents by Age

Age	amount	Presentation (%)
15 years	10	4.5
16 years	76	34.2
17 years	97	43.7

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18 years	39	17.6
Total	222	100

From table 1 shows that of 222 respondents, 15 years old 10 people (4.5%), 16 years old 76 people (34.2%), 17 years old 97 people (43.7%) and 39 years old 18 people (17.6%).

(2) Gender

Table 2. Distribution of Respondents by Gender Adolescents

Gender	amount	Presentation (%)
Male	194	87.4
women	28	12.6
Total	222	100

From table 2 shows that of 222 respondents who were male as many as 194 people (87.4%) and those who were female as many as 28 people (12.6%).

(3) Frequency of playing *online games*

Table 3. Distribution of Respondents Based on Frequency of Playing *Online Games* in Teens

Frequency of playing *online games*	amount	Presentation (%)
1	45	20.3
2	49	22.1
3	44	19.8
4	24	10.8
5	23	10.4
6	10	4.5
7	7	3.2
8	3	1.4
9	1	0.5
10	6	2.7
11	1	0.5
12	2	0.9
13	2	0.9
14	2	0.9
15	1	0.5
16	1	0.5
17	1	0.5
Total	222	100

From table 3 shows that the frequency of playing *online games* once a day is 45 people (20.3%), 2x a day 49 people (22.1%), 3 times a day 44 people (19.8%), 4 times a day 24 people (10.8) %), 5 times daily 23 people (10.4%), 6 times a day 10 people (4.5%), 7 times a day 7 people (3.2%), 3 times a day 3 people (1.4%), 9 times a day as many as 1 person (0.5%), 10 times a day as many as 6 people (2.7%), 11 times a day as many as 1 person (0.5%), 12 times a day as many as 2 people (0.9%), 13 times a day as many as 2 people (0.9%), 14 times a day for 2 people (0.9%), 15 times a day for 1 person (0.5%), 16 times a day for 1 person (0.5%) and 17 times a day for 1 person (0.5%).

(4) Long time playing *online games*

Table 4. Distribution of Respondents Based on Length of Playing *Online Games* in Teenagers

Long time playing *Online Games*	amount	Presentation (%)
1	16	7.2
2	26	11.7
3	24	10.8
4	26	11.7
5	18	8.1
6	21	9.5
7	11	5
8	17	7.7
9	8	3.6
10	11	5
11	3	1.4
12	10	4.5
13	2	0.9
14	2	0.9
15	3	1.4
16	2	0.9
17	6	2.7
18	1	0.5
19	4	1.8
20	4	1.8
21	7	3.2
Total	222	100

Source: primary data, 2019.

From table 4 shows that the frequency of playing *online games* a day, 1 hour is 16 people (7.2%), 2 hours is 26

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people (11.7%), 3 hours is 24 people (10.8%), 4 hours is 26 people (11.7 %), 5 hours of 18 people (8.1%), 6 hours of 21 people (9.5%), 7 hours of 11 people (5%), 8 hours of 17 people (7.7%), 9 hours of 8 people (3.6 %), 10 hours by 11 people (5%), 11 hours by 3 people (1.4%), 12 hours by 10 people (4.5%), 13 hours by 2 people (0.9%), 14 hours by 2 people (0.9 %), 15 hours of 3 people (1.4%), 16 hours of 2 people (0.9%), 17 hours of 6 people (2.7%), 18 hours of 1 person (0.5%), 19 hours of 4 people (1.8 %), 20 hours were 4 people (1.8%) and 21 hours were 7 people (3.2%).

(5) The level of attachment to *online games*

Table 5. Distribution of Respondents by Level of Attachment to *online games*

Level of Attachment with *Online Games*	amount	Presentation (%)
Moderate	117	52.7
Height	105	47.3
Total	222	100

From table 5 shows that of 222 respondents the level of attachment to *online games* in the moderate category was 117 people (52.7%) while those in the high category were 105 people (47.3%).

(6) Behavior

Table 6. Distribution of Respondents Based on Behavior in Adolescents

Behavior	amount	Presentation (%)
Aggressive Non aggressive	152 70	68.5 31.5
Total	222	100

From table 6 shows that of 222 respondents, 70 people (31.5%) did not behave aggressively and 152 people (68.5%) behaved aggressively.

4.3 Bivariate Analysis

From table 7 shows that out of 45 people who play *online games* once a day 12 people (26.70%) behave in an aggressive manner and 33 people (73.30%) who behave aggressively, out of 49 people who play *online games* 2 times a day that behaves non-aggressively as many as 18 people (36.70%) and who behaves aggressively as many as 31 people (63.30%), out of 44 people who play *online games* 3 times a day who behave non-aggressively as many as 8 people (18 , 20%) and those who behave aggressively as many as 36 people (81.20%), out of 24 people who play *online games* 4 times a day who behave non-aggressively as many as 7 people (29.20%) and who behave aggressively as many as 17 people (70.80%).

Table 7. Relationship of Frequency of Playing *Online Games* with Aggressive Behavior

Variable	Frequency (times)	Aggressive behavior		Total	P value
		Not aggressive	aggressive		
Frequency of Playing *Online Games*	1	12 26.70%	33 73.30%	45 100%	0871
	2	18 36.70%	31 63.30%	49 100%	
	3	8 18.20%	36 81.20%	44 100%	
	4	7 29.20%	17 70.80%	24 100%	
	5	12 52.20%	11 47.80%	23 100%	
	6	6 60.0%	4 40.0%	10 100%	
	7	3 42.90%	4 57.10%	7 100	
	8	2 66.70%	1 33.30	3 100%	
	9	1 100%	0 0.00%	1 100%	
	10	0 0.00%	6 100%	6 100%	
	11	0 0.00%	1 100%	1 100%	
	12	0 0.00%	2 100%	2 100%	
	13	0 0.00%	2 100%	2 100%	
	16	0 0.00%	2 100%	2 100%	
	17	0 0.00%	1 100%	1 100%	
	18	1 100%	0 0.00%	1 100%	
	20	0 0.00%	1 100%	1 100%	
Total		70 31.50%	152 68.50%	222 100%	

From 23 students who play *online games* as much as five times a day behaving aggressively as many as 12 people (52.20%) and who behave aggressively as many as 11 people (47.80%), of the 10 people who play *online games* 6 times a day that do not behave aggressively as many as 6 people (60%) and who behave aggressively as many as 4 people (40%), out of 7 people who play *online games* 7 times a day who behave non-aggressively as many as 3 people (42.90%) and who behave aggressively as much 4 people (57.10%), out of 3 people who play *online games*

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8 times a day who behave non-aggressively as many as 2 people (66.70%) and who behave aggressively as many as 1 person 9 (33.30%), from 1 person who played *online games* 9 times a day who did not behave aggressively as many as 1 person (100%), out of 6 people who played *online games* 10 times a day who behaved a magnitude of 6 people (100%).

Table 8. Correlation the Length Play *Online Games* with Aggressive Behavior

Variable	Length (Hours)	Aggressive behavior		Total	P value
		Not aggressive	aggressive		
Length Playing Game Online	1	8 50.0%	8 50.0%	16 100%	0,000
	2	19 73.10%	7 26.90%	26 100%	
	3	11 45.80%	13 54.20%	24 100%	
	4	11 42.30%	15 57.70%	26 100%	
	5	5 27.80%	13 72.20%	18 100%	
	6	2 9.50%	19 90.50%	21 100%	
	7	3 27.30%	8 72.70%	11 100	
	8	7 41.20%	10 58.80%	17 100%	
	9	0 0.00%	8 100%	8 100%	
	10	1 9.10%	10 90.90%	11 100%	
	11	0 0.00%	3 100%	3 100%	
	12	2 20.00%	8 80.00%	10 100%	
	13	0 0.00%	2 100%	2 100%	
	14	0 0.00%	2 100%	2 100%	
	15	0 0.00%	3 100%	3 100%	
	17	0 0.00%	2 100%	2 100%	
	20	0 0.00%	6 100%	6 100%	
	21	0 0.00%	1 100%	1 100%	
	22	0 0.00%	4 100%	4 100%	
	23	1 25.00%	3 75.00%	4 100%	
	24	0 0.00%	7 100%	7 100%	
Total		70 31.50%	152 68.50%	222 100%	

From 1 people who play *online games* 11 times a day that behaves aggressively as many as 1 (100%), from 2 people who play *online games* as much as 12 times a day that behaves aggressively as much as 2 (100%), from 2 people who play the game online as many as 13 times a day who behave aggressively by 2 people (100%), out of 2 people who play *online games* as much as 16 times a day who behave aggressively as much as 2 people (100%), from 1 person who plays *online games* 17 times a day who behaves 1 person aggressive (100%), from 1 person who plays *online games* 18 times a day who behaves non-aggressively by 1 person (100%), from 1 person who plays *online games* 20 x a day who behaves aggressively by 1 person (100%). The probability value of this variable is 0.871.

Table 8 shows that out of 16 people who play *online games* 1 hour a day who behave non-aggressively as many as 8 people (50%) and who behave aggressively as many as 8 people (50%), out of 26 people who play online games 2 hours a day who behave not aggressive as many as 19 people (73.10%) and those who behave aggressively as many as 7 people (26.90%), out of 24 people who play online games 3 hours a day who behave non-aggressively as many as 11 people (45.80%) and who 13 people behave aggressively (54.20%), out of 26 people who play online games 4 hours a day who behave non-aggressively by 11 people (42.30%) and those who behave aggressively by 15 people (57.70%), from 18 people who play online games 5 hours a day who behave non-aggressively as many as 5 people (27.80%) and who behave as much as 13 people (72.20%).

From 21 people who play online games for 6 hours a day behaving aggressively as much as 2 (9.50%) and who behave Agree shifts as many as 19 people (90.50%), from 11 people who play online games for 7 hours a day 3 people (27.30%) who did not behave aggressively and 8 people (72.70%) behaved aggressively, out of 17 people who played online games 8 hours a day who behaved 7 people (41.20%) and those who behave aggressively as many as 10 people (58.80%), out of 8 people who play online games 9 hours a day and those who behave aggressively as many as 8 people (100%), out of 11 people who play online games 10 hours a day who behave non-aggressively as many as 1 person (9.10%) and those who behave aggressively as many as 10 people (90.90%), out of 3 people who play online games 11 hours a day who behave aggressively as many as 3 people (100%), out of 10 people who play games online 12 hours a day who behave non-aggressively as many as 2 people (20%) and who behave aggressive as many as 8 people (80%), out of 2 people who play online games 13 hours a day who behave in an aggressive manner as many as 2 people (100%).

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From 2 people who play online games 14 hours a day who behave aggressively as much as 2 (100%), from 3 people who play online games 15 hours a day who behave aggressively as many as 3 people (100%), from 2 people who play online games 17 hours a day who behave aggressively by 2 people (100%), from 6 people who play online games 20 hours a day who behave aggressively by 6 people (100%), from 1 person who plays online games 21 hours a day who behaves aggressively by 1 people (100%), from 4 people who play online games 22 hours a day who behave aggressively as many as 4 people (100%), out of 4 people who play online games 23 hours a day who behave non-aggressively by 1 person (25%) and who aggressive behavior as many as 3 people (75%), out of 7 people who play online games 24 hours a day who behave aggressively as many as 7 people (100%). The probability value of this variable is 0,000.

Table 9. Relationship between the levels of attachment to online games with aggressive behavior

Variable	The level of attachment to online games	Aggressive Behavior		Total	Pvalue
		Not aggressive	aggressive		
Level of Attachment with Online Games	Is	60 51.30%	57 48.70%	117 100%	0,000
	High	10 9.50 %%	95 90.50%	105 100%	
Total		70 31.50%	152 68.50%	222 100%	

Table 9 shows that out of 117 people who engaged in online gaming in the medium category, 60 people (51.30%) behaved in an aggressive manner and 57 people (48.70%) who behaved aggressively, out of 105 people who were connected. with online games in the high category, 10 people (9.50%) did not behave aggressively and 95 people (90.50%) behaved aggressively. The probability value of this variable is 0, 00.

4.4 Multivariate Analysis

Summary Model			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	206,693 [a]	.271	.380
Estimation is terminated at iteration number 5 because the parameter estimate is changed by less than.001.			

The *Model Summary* table above, it can be seen that the model by entering independent variables turns out to be a difference in the estimation of its parameters (-2 Log likelihood) of 206,693 points. If seen, the value of R Square of 27, 1 % (Cox & Snell) and 38.0% (Nagelkerke). Thus, the bias is interpreted that the proportion of variance diagnosed with aggressive behavior that is commonly explained by the frequency of playing online games, the length of playing online games and the level of attachment to online games is 38.0%.

Hosmer and Lemeshow Test			
Step	Chi-square	df	Sig.
1	3,286	8	.915

The *Hosmer and Lemeshow Test* table explains that the Chi-square test value obtained was 3.286 with a value of p = 0.915. The meaning of this value is to accept the null hypothesis with the following hypothesis:

Ho: The model has sufficiently explained the data (*Godless of Fit*)

Ha: The model does not adequately explain the data

So, with a value of p = 0.915> 0 , 05 , it can be concluded that the null hypothesis is accepted meaning the model has sufficiently explained the data.

Variables in the Equation									
		B	SE	Wald	df	Sig.	Exp (B) Lower	95% CIfor Exp (B)	
								Upper	
Step 1[a]	Frequency Playing Game Online	-284	.082	12,036	1	.001	753	642	.884
	Length Game Online	.239	.062	15,047	1	.000	1,270	1,126	1,434
	Game Online Levels (1)	-1.495	.440	11,528	1	.001	.244	.095	.532
	Constant	1,325	.508	6,808	1	.009	3,763		

The variable frequency of playing online games has a value of p = 0.001 <0, 05, the variable length of playing online games has a value of p = 0,000 <0.05 and the vari-

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able level of attachment to online games has a value of $p = 0.001 < 0.05$, which means that there is a relationship between frequency, length of time playing online games and the level of attachment to online games with aggressive behavior in adolescents of class XI in V State Vocasional 3 Jayapura. For the risk of each independent variable, it is seen from the value of Exp (B), with the following results:

(1) Variable frequency of online game play, OR value of frequency of online game play is 0.753 less than 1, so it is a protective and significant factor because the *Lower* value is 0.642 and *Upper* 0.884 does not contain a value of 1.

(2) Variable length of playing online games , OR Value old variable playing online games is 1,270 greater than 1 so it is a risk factor and significant because the value of *Lower* 1.126 and *Upper* 1.434 does not contain a value of 1. This can mean that people who have long played online games have a risk of 1.126 times to behave aggressively compared to people who play their online games fast.

(3) Variable level of attachment to online games , OR value The level of attachment to online games is 0.224 less than 1, so it is a protective and significant factor because the value of *Lower* 0.095 and *Upper* 0.532 does not contain a value of 1.

5. Discussion of study

(1) Frequency of playing online games.

Based on table 5 it can be explained that the frequency distribution of playing online games for class XI teenagers is 1 x daily as many as 45 people (20.3%), twice daily 49 people (22.1%), 3 x daily as many as 44 people (19.8%), 4 x 24 people a day (10.8%), 5 times a day 23 people (10.4%), 6 times a day 10 people (4.5%), 7 times a day 7 people (3.2%), 8 times a day 3 people (1.4 %), 9 times a day as many as 1 person (0.5%), 10 times a day are 6 people (2.7%), 11 times a day are 1 person (0.5%), 12 times a day are 2 people (0.9%), 13 times a day 2 people (0.9%), 14 times a day 2 people (0.9%), 15 times a day 1 person (0.5%), 16 times a day 1 person (0.5%) and 17 times a day 1 person (0.5%).

The average frequency of playing online games is 3,77 times a day and the total number of times playing online games is from 222 respondents 836 times a day. This is because online games are rampant and are known by all types of people. There are several factors that influence, namely, the availability of internet facilities at home, as well as the availability of internet cafes that provide 24 hours of gaming time.

(2) Long time playing online games.

From table 6 shows that the frequency of playing online games a day, 1 hour is 16 people (7.2%), 2 hours is 26 people (11.7%), 3 hours is 24 people (10.8%), 4 hours is 26 people (11.7 %), 5 hours of 18 people (8.1%), 6 hours of 21 people (9.5%), 7 hours of 11 people (5%), 8 hours of 17 people (7.7%), 9 hours of 8 people (3.6 %), 10 hours by 11 people (5%), 11 hours by 3 people (1.4%), 12 hours by 10 people (4.5%), 13 hours by 2 people (0.9%), 14 hours by 2 people (0.9 %), 15 hours of 3 people (1.4%), 16 hours of 2 people (0.9%), 17 hours of 6 people (2.7%), 18 hours of 1 person (0.5%), 19 hours of 4 people (1.8) %), 20 hours were 4 people (1.8%) and 21 hours were 7 people (3.2%).

The average length of playing online games is 7, 34 hours per day and the total length of playing online games from 222 respondents is 1630 hours each day. There are several factors that affect a person playing a long time online games are the lack of attention from the people closest to them and the lack of activities that sometimes make online games a sought-after escape.

(3) The level of attachment to online games.

From table 7 shows that of 222 respondents the level of attachment to online games in the moderate category was 117 people (52.7%) while those in the high category were 105 people (47.3%). There are several factors that affect a person's level of attachment to online games, namely, depression, lack of control and lack of environmental activities and parenting from parents.

According to Soleman, 2010 playing online games can have a negative impact both socially, psychologically and physically. Socially, relationships with friends and family become tenuous because their time together becomes less and makes someone less concerned about the things that happen around us [14]. It also makes it so closed that it is difficult to express them when in a real environment. Psychologically, a person's mind becomes constantly thinking about the game being played. His feelings will become anxious, frustrated and angry when not playing games. Physically, it will disrupt his health. Someone will forget to eat when they are too enjoying the game. Body health decreases due to lack of exercise and becomes easily tired when doing physical activity.

(4) Behavior.

Someone who has a level of attachment to online games will give a negative influence or effect on behavior. From table 8 shows that of 222 respondents, 70 people (31.5%) did not behave aggressively and 152 people (68.5%) behaved aggressively. According to Yee in 2010, someone who is bound by online games will become anxious, frustrated and angry when not playing games, feeling guilty when playing, continues to play even though

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they no longer enjoy and have problems in social life or relationships with others and in financial life.

(5) The relationship between the frequencies of playing online games with aggressive behavior.

From table 9 shows that out of 45 people who play online games once a day 12 people (26.70%) behave in an aggressive manner and 33 people (73.30%) who behave aggressively, out of 49 people who play online games 2 times a day that behaves non-aggressively as many as 18 people (36.70%) and who behaves aggressively as many as 31 people (63.30%), out of 44 people who play online games 3 times a day who behave non-aggressively as many as 8 people (18 , 20%) and those who behave aggressively as many as 36 people (81.20%), out of 24 people who play online games 4 times a day who behave non-aggressively as many as 7 people (29.20%) and who behave aggressively as many as 17 people (70 , 80%).

From 23 people who play online games 5 times a day who behave non-aggressively as many as 12 people (52.20%) and who behave aggressively as many as 11 people (47.80%), out of 10 people who play online games 6 times a day who behave not aggressive as many as 6 people (60%) and those who behave aggressively as many as 4 people (40%), out of 7 people who play online games 7 times a day who behave non-aggressively as many as 3 people (42.90%) and who behave aggressively as much as 4 people (57.10%), from 3 people who play online games 8 times a day who behave non-aggressively as many as 2 people (66.70%) and who behave aggressively as many as 1 person 9 (33.30%), from 1 person who play online games 9 times a day who behave non-aggressively as many as 1 person (100%), out of 6 people who play online games 10 times a day who behave aggressively as many as 6 people (100%).

From 1 person who plays online games 11 times a day who behaves aggressively as much as 1 person (100%), from 2 people who play online games 12 times a day who behaves aggressively as much as 2 people (100%), from 2 people who plays online games as many as 13 times a day who behave aggressively as many as 2 people (100%), from 2 people who play online games as much as 16 times a day who behave aggressively as many as 2 people (100%), from 1 person who plays online games 17 times a day who behaves aggressively as many as 1 person (100%), from 1 person who plays online games 18 times a day who behaves non-aggressively by 1 person (100%), from 1 person who plays online games 20 x a day who behaves aggressively by 1 person (100%).

From the logistical test results obtained are not meaningful results where the value of p 0.871> 0, 05 then Ha is rejected. This means that there is no influence between the frequencies of playing online games with aggressive behavior or there are other factors that influence aggressive behavior in class XI adolescents in Vocational State 3 Jayapura Elementary School. This study is in line with Fitrotun and Kustiningsi (2017) about the relationship between the frequency of playing online games with aggressive behavior in XI IPS adolescents at Muhammadiyah 7 High School in Yogyakarta with p = 0.066 (0.066> 0.05). This means there is no relationship between the frequencies of playing online games with the aggressive behavior of teenagers because there are still many other factors.

The OR value of the frequency of playing online games is 0.753 smaller than 1, so it is a protective and significant factor (significant) because the value of *Lower* 0.642 and *Upper* 0.884 does not contain a value of 1. Protective factor (protective factor) is a term used to refer to a balancing factor or one that protect against risk factors (factors that give rise to risk). This means that the frequency of playing online games can work or can help if someone has got a risk factor, so as to reduce the risk factor.

The factors that influence so that in this study makes the frequency of playing online games have no influence on the aggressive behavior of adolescents is because teens who play online games are high frequency (many times a day) but the time or duration is only short (only a few hours even only in minutes count) is inversely proportional to students whose frequency of playing online games is short but the duration or time is very long.

Based on Sarwono in 2014, there are several factors that cause a person to behave aggressively including, social (environment), personal (personal individual), culture, situational, mass media and domestic violence. Meanwhile, according to Koeswara (2013), the factors that cause aggressive behavior are poverty, air temperature, and the role of violent learning, frustration, generational inequality, anger, erroneous disciplinary processes and biological factors [15].

(6) Old relationship playing online games with aggressive behavior

There are 16 samples who play online games 1 hour a day who behave non-aggressively as many as 8 people (50%) and who behave aggressively as many as 8 people (50%), out of 26 people who play online games 2 hours a day who behave not aggressive as many as 19 people (73.10%) and those who behave aggressively as many as 7 people (26.90%), out of 24 people who play online games 3 hours a day who behave non-aggressively as many as 11 people (45.80%) and who 13 people behave aggressively (54.20%), out of 26 people who play online games 4 hours a day who behave non-aggressively by 11 people (42.30%) and those who behave aggressively by 15 peo-

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ple (57.70%), from 18 people who played online games 5 hours a day who did not behave aggressively as many as 5 people (27.80%) and who behaved aggressively as many as 13 people (72.20%).

From 21 people who play online games 6 hours a day who behave non-aggressively as many as 2 people (9.50%) and who behave aggressively as many as 19 people (90.50%), out of 11 people who play online games 7 hours a day who behave no aggressive as many as 3 people (27.30%) and those who behave aggressively as many as 8 people (72.70%), out of 17 people who play online games 8 hours a day who behave non-aggressively as many as 7 people (41.20%) and who behave aggressive as many as 10 people (58.80%), from 8 people who play online games 9 hours a day and those who behave aggressively as many as 8 people (100%), out of 11 people who play online games 10 hours a day who behave non-aggressively as much as 1 person (9.10%) and those who behave aggressively as many as 10 people (90.90%), out of 3 people who play online games 11 hours a day who behave aggressively as many as 3 people (100%), out of 10 people who play online games 12 hours a day who behaves non-aggressively as many as 2 people (20%) and who behave aggressive as many as 8 people (80%), from 2 people who play online games 13 hours a day who behave aggressively as many as 2 people (100%).

From 2 people who play online games 14 hours a day who behave aggressively as many as 2 people (100%), from 3 people who play online games 15 hours a day who behave aggressively as many as 3 people (100%), from 2 people who play online games 17 2 hours a day who behave aggressively by 2 people (100%), from 6 people who play online games 20 hours a day who behave aggressively by 6 people (100%), from 1 person who plays online games 21 hours a day who behaves aggressively by 1 person (100%), from 4 people who play online games 22 hours a day who behave aggressively by 4 people (100%), from 4 people who play online games 23 hours a day who behave non-aggressively by 1 person (25%) and who behave aggressive as many as 3 people (75%), from 7 people who play online games 24 hours a day who behave aggressively as many as 7 people (100%).

From the Logistic test results obtained meaningful results where the value of p = 0, 00 <0.05 then Ha is accepted. This means that there is an influence or relationship between the lengths of playing online games with the aggressive behavior of teenagers in class XI Vocational school 3 Jayapura. These results indicate that there is a positive relationship between the lengths of playing online games with the aggressive behavior of adolescents. This means that the old variable playing online games can be used as a trigger to predict the emergence of aggressive teenage behavior. The higher the length of playing online games, the higher the aggressive behavior of teenagers, conversely the lower the longer playing online games, the lower the aggressive behavior of teenagers.

The length of playing online games gives enough influence in measuring the aggressive behavior of teenagers. This is because the magnitude of the effective contribution of time playing online games against juvenile aggressive behavior seen $r^2 = 0.222$ or 22, 2 %, so long playing online games can show the effect of the measure aggressive behavior of teenagers. This shows that there are 77,8 % of other variables that influence adolescent aggressive behavior, outside the old variable playing online games. These variables include biological, psychological, anger, situational, environmental, social, role models of violence, generation disparities and erroneous disciplinary factors.

The OR value of the old variable playing online games is 1,270 greater than 1 so it is a risk factor and is significant because the *Lower* 1.126 and *Upper* 1.434 values do not contain a value of 1. This means that people who have long played online games have a risk of 1.126 times to behave aggressively compared to people who play online games are lacking or fast.

The results of this study are consistent with the opinions expressed by Anis Tiani (2014) saying there is a very significant positive relationship between playing online games with aggressive behavior. Effective contribution is between variables playing online games with children's aggressive behavior by 61%.

The results of this study turned out to be a positive relationship between the lengths of playing online games with the aggressive behavior of adolescents who have a long time playing online games that are high in teens will tend to behave aggressively. This is because adolescents are good observers, so adolescents tend to want to do mental activities that are focused on real objects or events.

Bandura 2007 states that is aggressing behavior is the result of social learning processes through observation of the social world. By watching the violence scene for a long time, the learning process of the violent model resulted in aggressive behavior [16]

(7) Relationship between the levels of attachment to online games with aggressive behavior.

Table 11 shows that out of 117 people who engaged in online gaming in the medium category, 60 people (51.30%) behaved in an aggressive manner and 57 people (48.70%) who behaved aggressively, out of 105 people who were connected. with online games in the high category, 10 people (9.50%) did not behave aggressively and

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95 people (90.50%) behaved aggressively.

From the Logistic test results obtained meaningful results where the value of p = 0, 00 <0.05 then Ha is accepted. This means that there is an influence or relationship between the levels of attachment to online games with the aggressive behavior of teenagers in class XI in Negeri 3 Jayapura. These results indicate that there is a positive relationship between the levels of attachment to online games with aggressive behavior of adolescents. This means that the variable level of attachment to online games can be used as a trigger to predict the emergence of aggressive behavior in adolescents. The higher the level of attachment, the higher the aggressive behavior of adolescents, conversely the lower the level of attachment, the lower the aggressive behavior of adolescents.

The level of attachment to online games gives enough influence in measuring the aggressive behavior of adolescents. This is because the amount of effective contribution of the level of online game attachment to adolescent aggressive behavior seen $r^2 = 0.276$ or 27, 6 % so that the level of online game attachment can show the effect in measuring the aggressive behavior of adolescents. This shows that there are 72 , 4 % of other variables that influence adolescent aggressive behavior, attachment level variables outside of online games. These variables include biological, psychological, anger, situational, environmental, social, role models of violence, generation disparities and erroneous disciplinary factors.

The OR value of the variable level of attachment to online games is 0.224 less than 1, so it is a protective and significant factor because the value of Lower 0.095 and Upper 0.532 does not contain a value of 1. Protective factor (protective factor) is a term used to refer to a balancing factor or that protects it from risk factors (factors that give rise to risk). This means the level of attachment to online games can work or can help if someone has got a risk factor, so as to reduce the risk factor.

The results of this study turned out to be in accordance with the opinion expressed by Merita (2015) which says that there is a relationship between online game addiction and aggressive behavior. The results of this study are also linked to *social learning theory* which states that an aggressive playing an online game, a right to stimulate aggressive behavior as adolescents will imitate what they see when playing games online [17].

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ARTICLE

Deep Learning in Medical Imaging and Drug Design

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ABSTRACT

Over the last decade, deep learning (DL) methods have been extremely successful and widely used in almost every domain. Researchers are now focusing on the convergence of medical imaging and drug design using deep learning to revolutionize medical diagnostic and improvement in the monitoring from response to therapy. DL a new machine learning paradigm that focuses on learning with deep hierarchical models of data. Medical imaging has transformed healthcare science, it was thought of as a diagnostic tool for disease, but now it is also used in drug design. Advances in medical imaging technology have enabled scientists to detect events at the cellular level. The role of medical imaging in drug design includes identification of likely responders, detection, diagnosis, evaluation, therapy monitoring, and follow-up. A qualitative medical image is transformed into a quantitative biomarker or surrogate endpoint useful in drug design decision-making. For this, a parameter needs to be identified that characterizes the disease baseline and its subsequent response to treatment. The result is a quantifiable improvement in healthcare quality in most therapeutic areas, resulting in improvements in quality and life duration. This paper provides an overview of recent studies on applying the deep learning method in medical imaging and drug design. We briefly discuss the fields related to the history of deep learning, medical imaging, and drug design.

1. Introduction

Even though deep learning algorithms exist for over a decade, their applications to solve real-world problems were very slow due to limited data and hardware computational power. Its booms started in 2016 when a model built using a deep learning algorithm (Alpha Go) beat the world champion player of Go[1]. This rejuvenates the researchers' interest in using deep learning algorithms to solve their various domain problems, especially in medical imaging and drug design.

Deep learning is an extension of an artificial neural network (ANN) that has been around for over three decades. This network work is based on mimicking human brain neurons [1]. An ANN is a shallow network consisting of an input layer, a single hidden layer, and an output layer, as shown in Fig.1. Each node in the input layer corresponds to a feature that is sent to the hidden layers. Upon

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receiving the features (data), the hidden layer performs some computation on the data and transfers them to the output layer, where results are generated. The difference between target output values and the desired output value is calculated using the back-propagation algorithm [2]. These errors are propagated back to the input, and weight adjustment is mostly made using stochastic gradient descent [3]; this process continues until the error is negligible. Deep learning has drastically increased machine learning algorithms' performance, primarily due to the reduction or complete elimination of feature engineering [4] as shown in Fig.2. The algorithms can extract features themselves and use those extracted features to either predict, classify, or cluster depending on the task performed. Recent development of computing capabilities, especially graphics processing units (GPUs) used in speeding up the complex calculations performed by the various algorithms, helps increase deep learning algorithms [5].

Advancement of technology, data availability, and improvement of existing algorithms are vital factors for the recent success of deep learning [4].

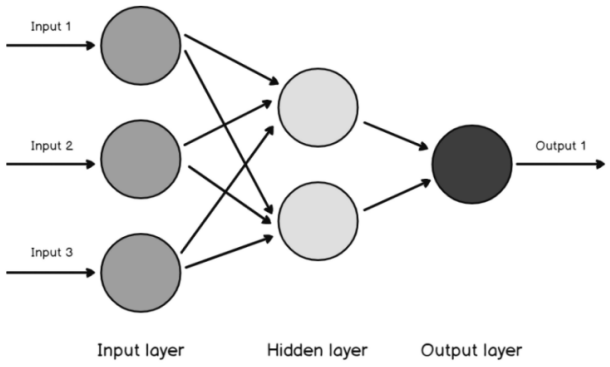

Figure 1. Artificial neural network

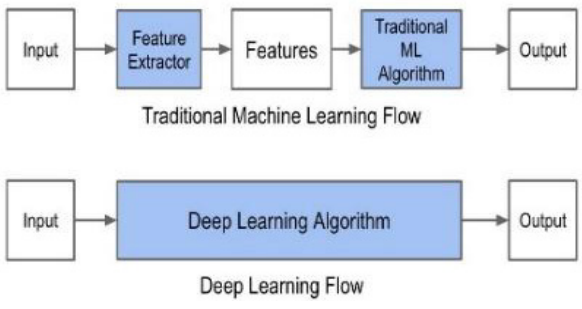

Figure 2. Machine learning vs Deep Learning

The ability to build a deep network with hundreds of hidden layers and millions of neurons give deep learning an edge over ANN, which mostly fails with more than four (4) hidden layers. Deep learning models have hyper-parameters such as activation function, learning rate, hidden layers, and many neurons which are essential factors to consider while designing your model. For medical images and drug discovery, the common activation function used is a rectified linear unit (RELU) [6]; in some instances, it variant like leaky RELU [7] is used. Model overfitting poses a significant challenge while training a deep network. Most of the models face this challenge where they learned all the features during the training but fails to perform the task during testing, i.e., using different datasets with the one used during the training. Regularization [8] and dropout [9] are commonly used techniques to reduce overfitting to solve this problem.

To test the robustness of deep learning, many researchers have built different models, one with machine learning and the other with deep learning, and used the same datasets to compare their performance. Various impressive results were obtained from the investigation conducted by [10-12] that deep learning models do not have superior performance over their machine learning counter fact without a large amount of training data. These experiments have shown that deep learning models performed better with a large number of training datasets.

Convolutional Neural Network (CNN) [13], Deep Belief Network (DBN) [14], Sparse and Variable Auto encoders [15] are among the commonly used deep learning algorithms in medical images and drug discovery. Selecting an algorithm depends on the task you want to perform. For medical image classification, different researchers used different architecture. The model proposed by [15] used CNN, and Auto encoders are used on the one proposed by [16]. Similarly, Auto encoders are used in drug discovery in the model proposed [17]. Generally, CNN is the most widely used architecture for image classification due to the robustness of pooling layers, and integrating dropout in the network has substantially decrease overfitting.

Even though Bayesian Network [18], Decision Tree [19], and Support Vector Machine (SVM) [20] are the most commonly used machine learning algorithms for drugs design and discovery, as shown in Fig. 3; recent trends of deep learning made it possible to make a substantial inroad to be among the algorithm used in drug discovery [1]. CNN, Autoencoders, Recurrent Neural Network (RNN), and other generative models are algorithms used in drug discovery and design [21-22].

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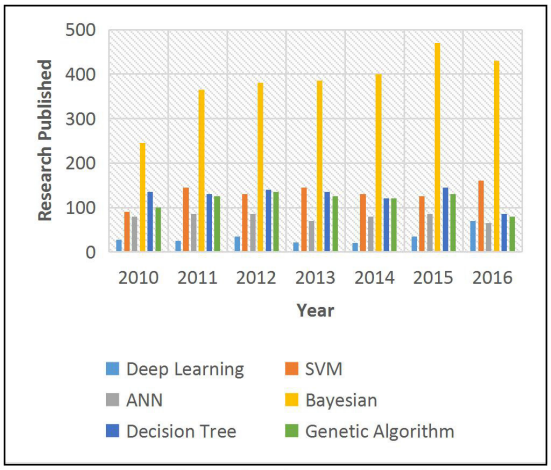

Figure 3. Analyzing the total number of publications using different machine learning algorithm for drugs design and discovery

2. Deep Learning in Medical Imaging

In a comparative analysis, deep learning models used in medical image analysis outperformed their counter fact of machine learning in anomaly detection, localization, image registration, segmentation, and diagnosis.

Most of the proposed medical image models are supervised learning based in nature; as such, annotated training data from experts are required to train them. Regrettably, obtaining training data in medical imaging is time-consuming, costly, and prone to errors. Furthermore, each medical image field has a separate template of the training process. This limitation has hindered the progress of the application of deep learning in medical images for years. The limitation was eliminated by the research performed by [23]. They proposed a general learning model that automatically extracts image pixel features; their model is flexible enough to be applied to any medical image field.

Clear separation of healthy and unhealthy body organs makes medical image segmentation one of the areas that received high research attention. Moreover, segmentation accuracy is the precursor of successful diagnosis and prevention. As such, various automated models were proposed to this effect [24]. The model proposed by [25] used automated image processing and clustering algorithms (K-means and expectation-maximization) to segment brain tumor. To improve spatial-temporal consistency of cardiac MRI segmentation, a hybrid spatio-temporal network (HST-Net) was proposed by [26]. Segmentation of children brain (from birth to age of 5) using MRI imaging is considered challenging to perform mainly due to noise increase, high volume effect, and minimization of tissue content [27], a CNN architecture model proposed by [28] to segment children brain solved the problems. The model proposed by [29] used both 2D and 3D CNN architecture to perform end-to-end volumetric segmentation of cardiac images.

Lesion and abnormality detections are a source of concern to many researchers in medical imaging due to the images' misclassification. With deep learning, various classifiers are used to classify images using binary classification. The models proposed by [30-32] used DNN architecture to detect and classify coronary classification of vein artery, cerebral microbleeds and, healthy and unhealthy skins.

3. Deep Learning in Drug Design

Complex molecule structure makes drug discovery and designs a challenging task to perform by the researchers in pharmacology and cheminformatics. This complexity arises from the hidden features among the molecules and features extracted from the molecules with artificial neural network models like SVM, decision tree, and genetics algorithm, which is a further step toward simplifying the drug design and development process [33-34]. The recent advances in deep learning have reduced the complexity of discovering molecule structures and their relationship within a compound. The importance of revealing their compound structure in obtaining qualitative classifiers or quantitative structure-activity relationship (QSAR) models.

For years, earlier research in the drug design domain continued to use human engineering to handcrafted molecule features descriptors. Even though some successes were reported in [35-38], deep learning benefits, like directly learning high powerful features among the molecules, are missing. Researchers have question that remained unanswered for years; can molecule complexity and hidden features structure be resolve by shifting from human engineering features extraction to deep learning models? Hilton Group took the challenge and proposed the first deep learning model for drug design and won the Merck Kaggle challenge 2012 (https://www.kaggle.com/c/MerckActivity). Similarly, a collaborative work between Hilton Group and Google in the subsequent year led to many research papers on deep learning-based QSAR modeling using different DNN architecture to perform multiple tasks. To imitate compound and protein interaction, different weights are given to the compound and protein features. These features become the input of the first hidden layer; thus, the model training is accelerated. The amount of training data does not show any significant effect on model performance [39]. Using this technique, a DNN model for drug discovery called AtomNet was proposed

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by [40]. This model was the first to utilize deep CNN architecture to extract compound features in drug analysis and discovery. The back-bone of drug design lies in the feature identification of compound-protein interaction. A model that can predict this interaction and protein sequence generation was proposed by [41]. The reason for the difficulty of adapting deep learning in drug discovery has to do with molecules structure. The model proposed by [42] used several features and chemical properties to predict molecule structure in drug discovery. Their model has shown robust performance compared to the rest of the model in the same category. The model proposed by [17] was the first that used unsupervised learning in drug design. They used a seven-layer Generative Adversarial Network (GAN) to screen a compound. To differentiate their model from the traditional compound screening methods using QSAR, they extracted features from input molecular fingerprints and generated new fingerprints that they used for training and testing their model. Their model outperformed all the traditional QSAR compound, screening models.

4. Conclusion and Promising Future

As we explained in this paper, different deep learning models have been applied to different medical imaging and drug discovery tasks as depicted in Fig.4 , which have achieved high performance with huge training data availability. The same performance was not obtained with a small amount of training data. This has shown that the success of any deep learning model depends on data. Some researchers [43] view that ANN models have the same performance precedence as deep learning models without enough training data. The question researchers continue to ask is how to quantify the amount of enough training data, and this has become a topic of discussion among them. Even though various techniques like transfer learning are developed to mitigate the scarcity of training data, its effectiveness varies across different domains and tasks to perform. Similarly, hyper-parameters tuning, the number of hidden layers, and the type of activation function used are also difficult to decide because each model performs best using different activation function and hyper-parameters values.

Even though deep learning has achieved almost the same accuracies as a human being, especially in image classification and segmentation using well-annotated datasets [44-45], their full adaptation in compound structures domain like drugs design and discovery [45] is problematic due to high constraint of the number of input features the models accept especially RNN, CNN and Restricted Boltzmann Machine [47] architectures. Simultaneously, high-performance models that perform various medical imaging tasks with limited training data are absent. This has continued to slow down deep learning models on lung cancer, liver, and spinal code injuries.

In the final analysis, although many successes have been recorded of using deep learning in both medical imaging, drug design, and discovery, development and improvements of models that will perform well with a limited amount of data are in dire need. Furthermore, deep learning models that can extract disease structure from the medical image is highly needed in our health care system. Additionally, to solve the problem associated with deep learning in compound structure domains like drug design and discovery, there is a need to optimize model architecture that will automatically extract useful molecule features and infer that the compound's relationship can be easily observed. Models that can perform these tasks will out rightly speedup drug design and clinical trials, reducing the time taken to produce drugs.

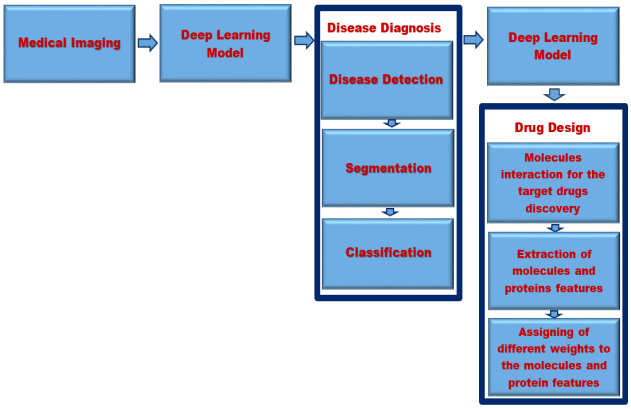

Figure 4. Application of Deep Learning from Medical Imaging to Drug Design

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