# Design of pharmacodynamic monitoring system based on acupuncture differential thermometry

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**Abstract**: To control drug effects by detecting temperature difference between biologically active point (BAP) and intact area of skin for treatment of mental illness, a device is developed for monitoring the temperature of BAP and the dose medication and its change in real time to increase effectiveness of treatment. Two electrodes by Foll R method are used and BAP is determined based on topographic anatomical reference points. The temperature values are measured by integral thermometers DS18B20. the received data are processed and temperature difference is calculated and displayed under the control of microcontroller Atmega32. The obtained data confirm the correlation between the temperature difference indicators BAP C7, Gi4 and neurological scales assessing severity of mental illness. The experimetal results show that the temperature difference can be criteria for evaluating the effects of drugs, which is the basis for computer control systems of of medical process of mental patients.

**Key words**: differential thermometry; biologically active points (BAP); monitoring drug effects

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## 0 Introduction

New psychotropic drugs can not fully solve the problem of optimal mental health treatment. The most important reason for reducing the effectiveness treatment of schizophrenia and depressive disorders is the emergence of drug resistance. To optimize the treatment of mental illness, it is necessary to use a device to determine the intensities at the beginning and in the end as well as the maximum intensity of each taking medication[1].

There are many different ways to assess drug effects, of which dynamic assessment of subjective sensations of the patient and objective signs of illness need additional examination methods. Each method evaluates the results of the treatment. The most appropriate method is acupuncture diagnosis. In this case, by recording one or another indicator of biologically active points (BAPs), the states of internal organs, functional systems and the whole organism can be evaluated because BAPs have a temperature difference from the surrounding skin[2].

Actual problem of psychiatry and clinical pharmacology on searching the ways and means to optimize the treatment of depression was solved by recording every second temperature difference between BAP C7, Gi4 and intact area of skin at a distance of 1—1.5 cm from BAPs using the microprocessor temperature logger, namely differential thermometry. The developed non-invasive method of monitoring psychotropic drug effects allows to monitor the status of regulatory processes of body after taking psychotropic drugs.

In Ref. [3] Fedorov B A described the possibility of measuring the temperature difference between the BAP and intact area of skin in a clinic. Using this approach, the authors showed the possibility of corrective treatment for mental patients. However, in this case, the changes in the functions of the meridian could not be established because only stationary status of BAP at a particular time was assessed[4]. In

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this paper this problem can be solved by recording the temperature difference between BAP and intact area of skin every second during 120 s.

## 1 System design

The thermopuncture device can find BAP, read the values of integral thermometer, calculate the temperature differences between BAPs and intact points, save the data in non-volatile memory with an option transfer to PC for further processing and long-term storage in a database[5]. Functionally it consists of searching BAP module, temperature measuring module, registration module of thermograms, LCD output module and microcontroller, as shown in Fig. 1.

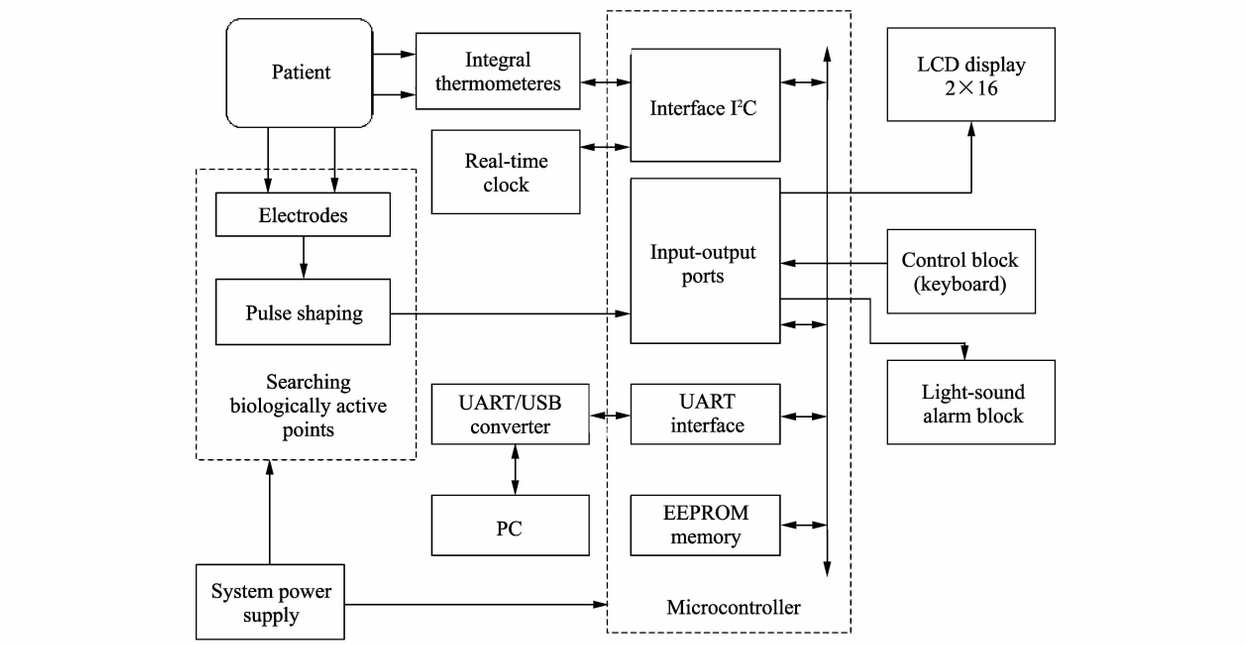


**Fig. 1 Block diagram of system structure**

BAPs can be found by using two electrodes—active and passive ones[6]. By controlling proposed device, resistance of the skin in place just as BAP is supposed to be found, can be etected easily and definitely.

The registration block processes the measurement data by integral thermometers, to convert the data to digital code and transmit them to microcontroller. The microcontroller processes received data, calculates temperature difference and displays the information on the display screen in real time for visual control $\Delta T$ of BAP. The recorded information in device memory via universal asychronous receiver-transmitter (UART) microcontroller can be transmitted to computer via universal serial bus (USB). The data are stored in computer in form of thermograms for detailed analysis and preservation in the database.

## 2 Hardware design

The core of this system is microcontroller ATMEGA32, and it contains all necessary interface modules for communication with peripheral components of the system, non-volatile electrically programmable memory (EEPROM) and UART with the necessary converters RS232 or USB for connection to PC. The microcontroller has been selected in order to modernize mobility and improve device, through a lot of work of temperature recorder, reducing the overall dimensions of the device and power consumption. It has the maximum capacity, low voltage and speed[7].

### 2.1 Microcontroller

Microcontroller provides a two-wire serial interface (TWI) for contact with digital thermometers ADT7420, which is designed to measure the skin surface temperature with an accuracy of ±0.2 ℃ in the temperature range from −10 to 85 ℃ with $U_s$ of 3 V, ultralow temperature drift of 0.007 3 ℃, power saving with 1 sample per second mode of 700 μW in normal mode and 7 μW in shutdown mode[8], as shown in Fig. 2.

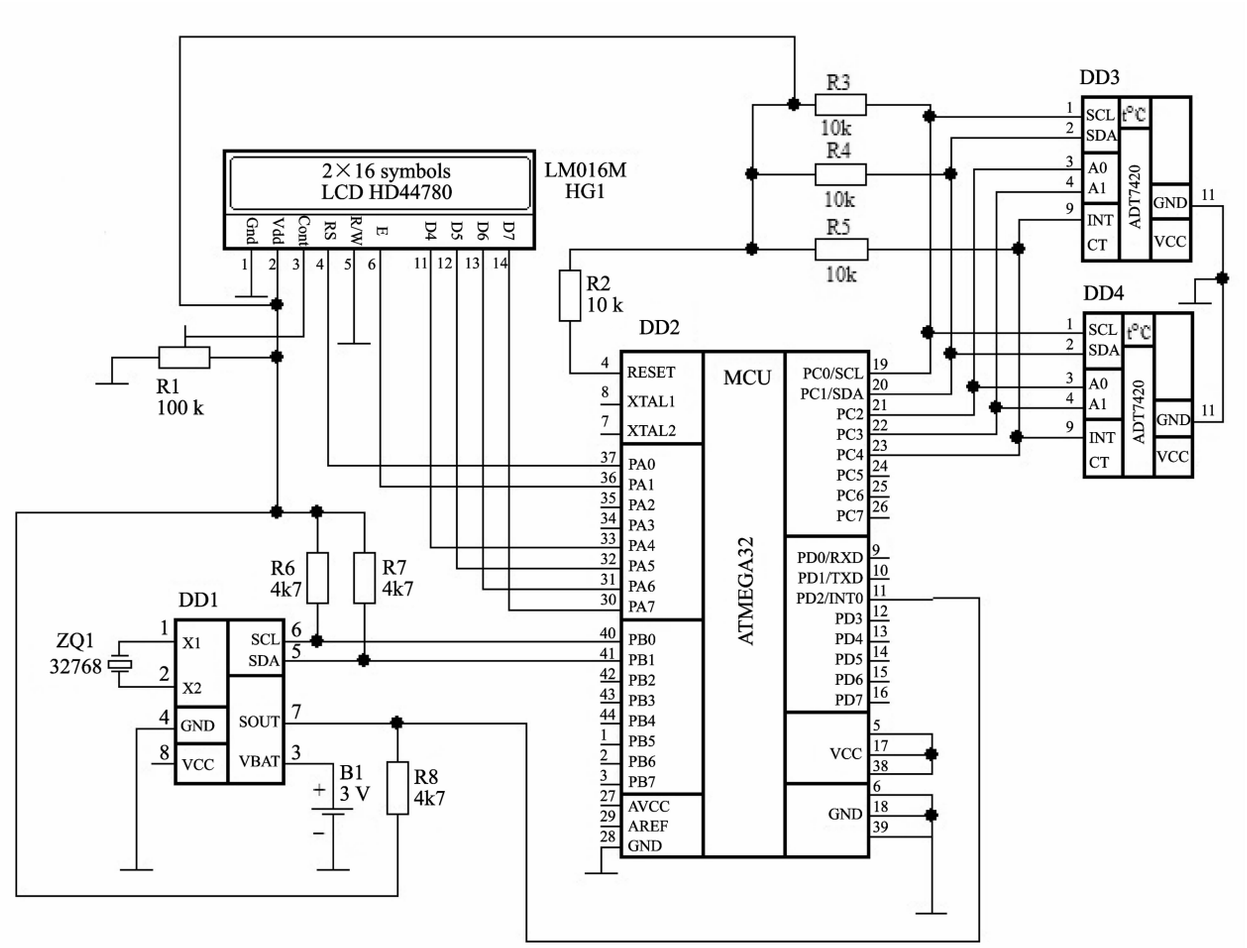


**Fig. 2 Connection diagram of microcontroller Atmega32**

Microcontroller provides a two-wire serial interface 2S for contact with real-time clock DS1307[3,7]. The date and time of medical research are simultaneously recorded to EEPROM together with the values of $\Delta T$ for each research. The input-output ports of microcontroller are connected for 2×16 LCD display (2 lines, 16 characters) for visual control of temperature by means of controller HD44780.

## 2.2 Searching BAP module

Searching BAP must keep smooth without any push to move the probe (active electrode) on the skin, holding the passive electrode in hand. As an indicator, searching BAP uses LED as signalization about finding biologically active point, as shown in Fig. 3.

The block of searching BAP generates a signal to microcontroller system, then microcontroller informs users of necessary messages about LCD display, sound and light alarms[4,9].

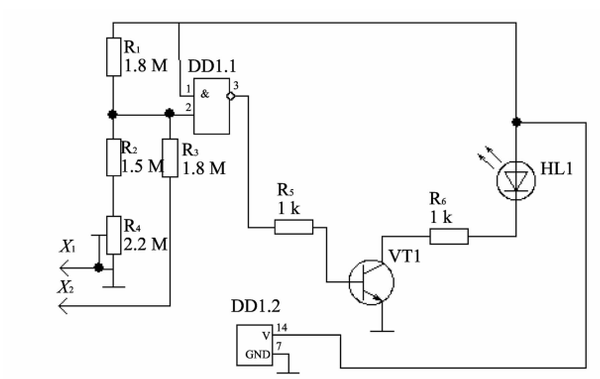


**Fig. 3 Schematic diagram of searching BAP**

## 2.3 Power supply

The supply voltage of the microcontroller, thermometeres, real-time clock and LCD is 3.3 V provided by stabilizer. Voltage supply for searching BAP block is 9 V. To convert the voltage from 3.3 to 9 V, an integrated DC/DC converter DA2 is used, as shown in Fig. 4.

For the purpose of patient safety from electrical

shock main power supply of this device, use a lithium-ion or lithium-polymer battery with the DC voltage of 3.6—3.7 V. Chip DA1 is controlled by battery charge signaled by the indicator that the battery is low, charged or absent. The battery of main power supply is charged by AC adapter only in a period when measurements are not performed on a patient[10].

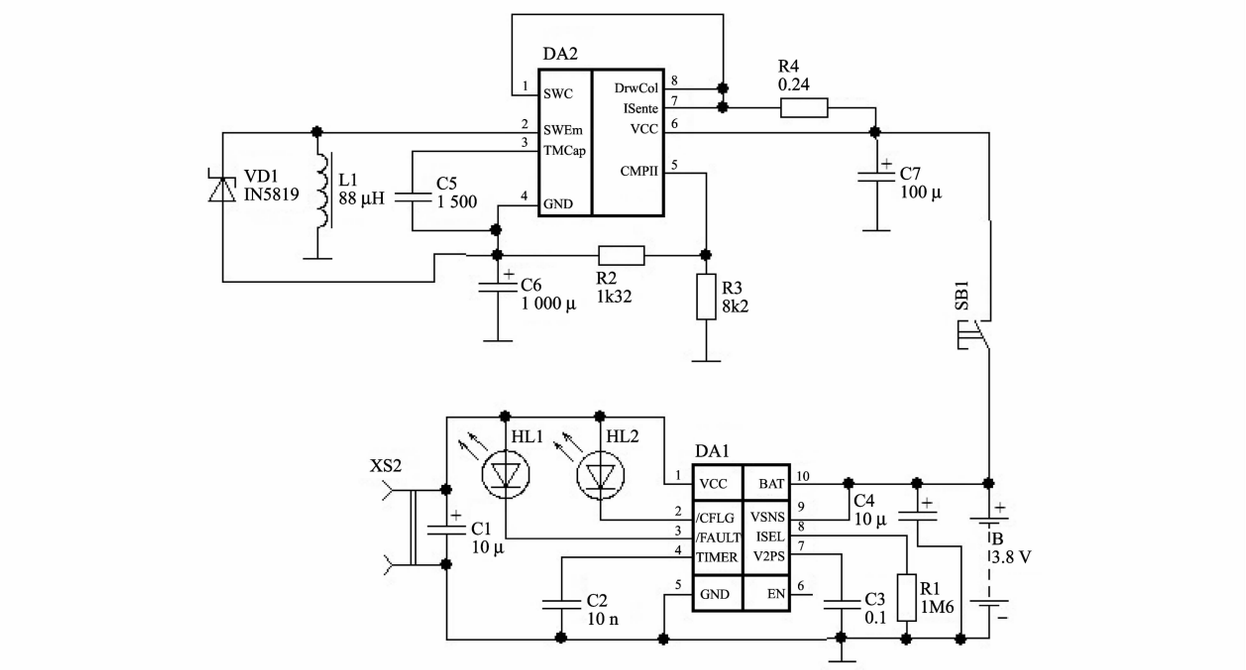


**Fig. 4 Schematics of power supply**

## 3 Software design

Programming is implemented using C language[11]. The flowchart is shown in Fig. 5.

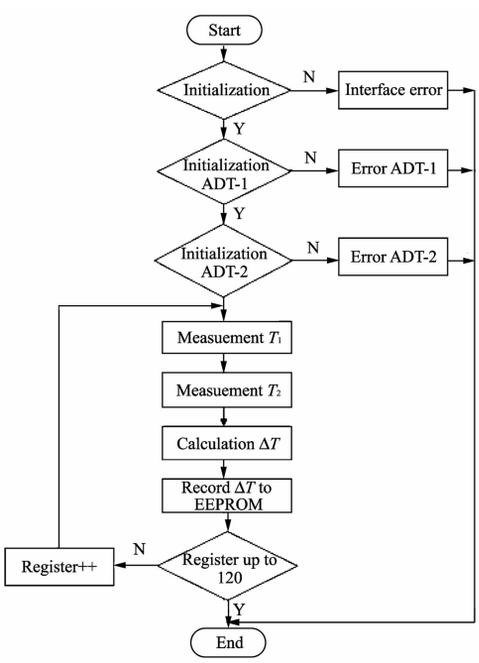


**Fig. 5 Flow chart of temperature measurement $\Delta T$**

Development software includes programming finding BAP and data processing, temperature measurement and temperature difference calculation, data output to LCD and program main menu screen.

## 4 Experiment results

To evaluate the drug effects in real time BAP C7, meridian of heart, and Gi4, meridian by means of large intestine[12], thermometry is consistently performed to all patients once a day simutaneady, at the same time, during 120 s, in the following order: 1) on the day of hospitalization, 2) on the 7th day, 3) on the 14th day of treatment. The obtained data were compared with the baseline data registered at admission to hospital.

All patients depending on the applied treatment were divided in two groups. The first group is control group, and the patients of this group received drugs for standard pharmacotherapy (SPT). The second group is the main group, and patients received SPT together with additional drug for the treatment of schizophrenia-flyuanksol[13].

Recorded data memory fixed in the form of graphs are displayed on the computer screen. To evaluate obtained thermograms, 14 indicators are used. At this stage, it can be found that the most sensitive parameters that reflect the chage of $\Delta T$ of BAP a 8 main indicators[14]:

1—The total number of positive and negative changes (TNPN);

2—The number of positive and negative changes in one minute (NPN/min);

3—The number of positive changes in one minute (NP/min);

4—The number of negative changes in one minute (NN/min);

6—The duration of the positive changes in one minute (DP/min);

7—The duration of the negative changes in one minute (DN/min);

13—The frequency of horizontal segments for one minute (FHS/min);

14—The length of horizontal segments for one minute (LHS/min).

Through mathematical data processing arithmetic mean (M), standard error of the arithmetic mean (± m) are calculated. The data is considered reliable with a significance level of $p<0.05$[15].

By analysis of indicators BAP C7 on the 7th day of treatment in both groups, similar changes are observed in indicators towards increase[16], as shown in Table 1.

**Table 1 Main indicators differential thermometry BAP C7 on the 7th and the 14th day**

| Indicators | BAP C7 | | | | | |
|---|---|---|---|---|---|---|
| | Control group | | | Main group | | |
| | 1st day | 7th day | 14th day | 1st day | 7th day | 14th day |
| 1 | 42±1.7 | 44.9±1.85 | 40.4±1.79 | 36.8±1.43 | 44.4±1.93* | 29.9±1.88* |
| 2 | 20.18±0.92 | 21.99±0.90 | 19.62±1.06 | 17.98±0,73 | 21.46±1.13* | 14.53±0.89* |
| 3 | 9.95±0.48 | 10.92±0.46 | 9.76±0.59 | 9.09±0.38 | 10.69±0.59* | 7.24±0.46* |
| 4 | 10.23±0.45 | 11.07±0.45 | 9.85±0.49 | 8.89±0.36 | 10.77±0.55* | 7.28±0.48* |
| 6 | 10.14±0.44 | 11.46±0.48 | 10.15±0.64 | 9.23±0.38 | 11.12±0.66* | 7.39±0.43* |
| 7 | 10.33±0.47 | 11.51±0.6 | 10.33±0.56 | 9.14±0.37 | 11.22±0.73* | 7.48±0.44* |
| 13 | 11.96±0.88 | 13.27±0.73 | 11.69±0.52 | 10.06±0.59 | 11.52±0.65 | 8.5±0.51 |
| 14 | 39.05±0.92 | 36.54±1.05 | 39.04±1.20 | 41.14±0.74 | 37.18±1.26* | 44,65±0,86* |

Note: * means $p<0.05$ compared with that on the 1st day

For the treatment only by a standard set of drugs based on the overall dynamics of the increase, significant difference is not obtained. For the indicators describing the process of meridian functioning only by standard pharmacotherapy, significant changes in treatment process are not fixed, as shown in Fig. 6.

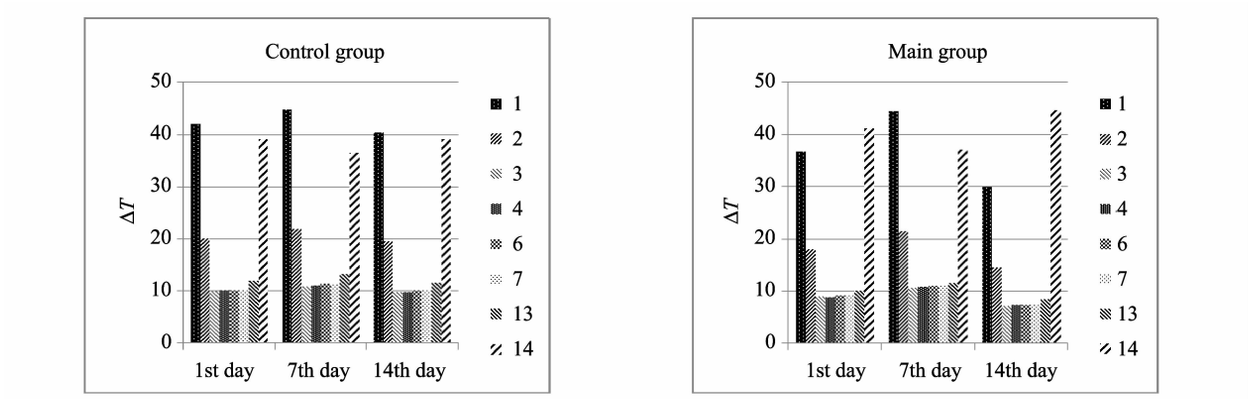


**Fig. 6 Dynamics of indicators differential thermometry BAP C7**

For the indicators of BAP Gi4 by differential thermometry in the control and the main groups up to

14 days, the main parameters on the 1st, 7th and 14th day are shown in Table 2.

**Table 2 Main indicators BAP Gi4 on the 7th and the 14th day by differential thermometry**

| Indicators | BAP Gi4 | | | | | |
|---|---|---|---|---|---|---|
| | Control group | | | Main group | | |
| | 1st day | 7th day | 14th day | 1st day | 7th day | 14th day |
| 1 | 31.6±1.63 | 36.8±1.75* | 33.3±1.69 | 32.55±1.63 | 39.56±1.77* | 45.56±2.10* |
| 2 | 15.36±0.77 | 17.86±0.76* | 16.19±0.9 | 15.76±0.66 | 19.01±0.82* | 22.15±1.11* |
| 3 | 7.59±0.43 | 8.88±0.42* | 7.98±0.49 | 7.88±0.34 | 9.5±0.38* | 11.07±0.56* |
| 4 | 7.81±0.35 | 8.98±0.35* | 8.2±0.43 | 7.88±0.33 | 9.5±0.47* | 11.08±0.56* |
| 6 | 7.93±0.46 | 9.09±0.39* | 8.3±0.41 | 8.14±0.4 | 9.83±0.48* | 11.34±0.63* |
| 7 | 7.97±0.43 | 9.32±0.44* | 8.39±0.47 | 8.23±0.44 | 10.05±0.71* | 11.29±0.58* |
| 13 | 11.41±0.71 | 11.94±0.59 | 11.2±0.65 | 9.37±0.6 | 10.86±0.57 | 12.38±0.67* |
| 14 | 31.58±0.88 | 29.05±0.81* | 30.8±1.07 | 43.14±0,9 | 39.65±1.18* | 36.88±1.20* |

Note: * means $p<0.05$ compared with that on the 1st day

On the 14th day in the treatment, the indicators of differential thermometry due to flyuankso continues to increase. In standard treatment group, increasing rate occurs on the 7th day, and then on the 14th day indicators return to the original tevel, without significant differences[17], as shown in Fig. 7.

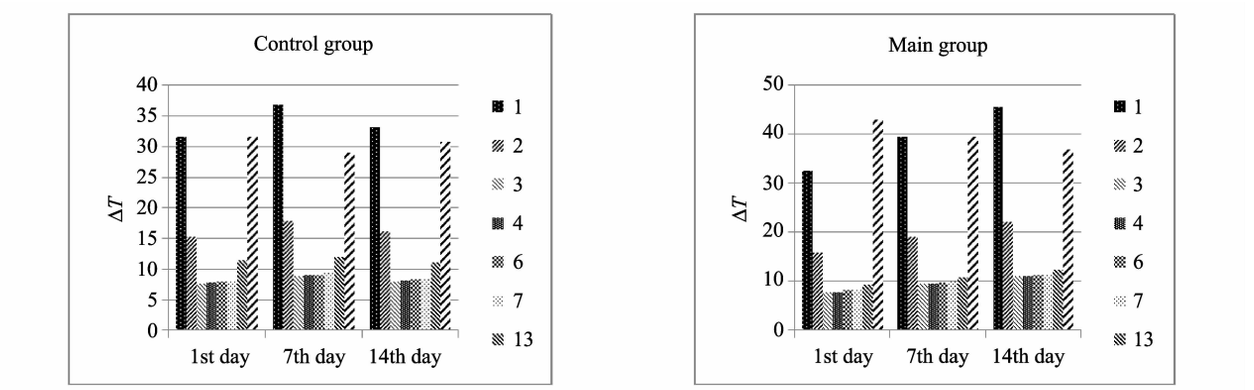


**Fig. 7 Indicators of BAP Gi4 by differential thermometry**

Evaluation of drug effects for the treatment of patients was conducted in view of both the data from temperature difference by thermometry and the evaluation of clinical and neurological scales[18]: national institute of health stroke scale (NIHSS) (Goldstein L B et al., 1989), the Original scale (Gusev E I et al., 2001), the scale of mental and emotional status of the feeling, activity, mood (FAM) (Doskin V A et al., 1973) and the scale of social adaptation Bartel (Bartel D W et al., 1965).

The analysis revealed that the severity of neurological deficit on the 14th day leveled in the control group only by standard treatment, as shown in Table 3.

**Table 3 Change in patients indicators of neurological status in control and main groups ($M\pm m$, $n=10$)**

| Scales | Control group | | Main group | |
|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment |
| NiHSS | 11.7±0.73 | 9.4±0.88* | 11.3±0.58 | 6.8±0.7* |
| Original | 36.5±1.09 | 38.6±1.23 | 37.2±1.13 | 42.5±1.35* |
| F | 2.09±0.14 | 3.45±0.26* | 2.09±0.12 | 4.15±0.29* |
| A | 2.26±0.1 | 3.52±0.24* | 2.24±0.13 | 4.22±0.25* |
| M | 2.01±0.11 | 3.45±0.29* | 2.23±0.18 | 4.29±0.31* |
| Bartel | 48.5±3.58 | 59.5±3.20* | 47.78±3.27 | 72.5±3.27* |

Note: * means $p<0.05$ the difference is valid compared with the values obtained before the treatment

On the NIHSS scale, overall total score decreased by 19.7% ($p<0.05$) and on the Original scale it increased only by 5.8% ($p<0.05$). The patients in the main group, the results of the recovery of neuro-

logical deficit are more important, the NIHSS scale overall score summary is decreased by 39.8% ($p<0.05$), on the original scale is increased by 14.2% ($p<0.05$).

In the course of statistical processing of the material, correlation analysis was carried out[19] between the changes in indicators of temperature difference between BAP and the dynamics of neurological status, psycho-emotional state and the level of quality of life, produced in the framework of the canonical analysis, describing the closeness of the relationship between the multidimensional elements of two sets of jointly distributed random variables. The rank coefficient of Spearman correlation is calculated by[20]

$$R_s = 1 - \frac{6\sum(D^2)}{n(n^2-1)},$$

where $n$ is number of ranked features (indicators of tested patients); $D$ is the difference between the ranks of two variables of each tested patients; and $\sum(D^2)$ the sum of squared differences ranks.

Correlation coefficient can vary within the range from 1 to $-1$. If the coefficient is close to 1, it means that both rows practically coincide, and if this ratio is close to $-1$, it is possible to speak about the complete inverse relationship.

In the course of the analysis, there is high correlation dependence in both groups, as shown in Table 4.

**Table 4 The overall results of canonical analysis of control and main groups**

| Control group | | | | | Main group | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Indicators | scales | C7 | scales | Gi4 | Indicators | scales | C7 | scales | Gi4 |
| Canonical significance $R_s$ | 0.999** | | 0.999** | | Canonical significance $R_s$ | 0.999** | | 0.989** | |
| Number of variables | 6 | 14 | 6 | 14 | Number of variables | 6 | 14 | 6 | 14 |

Note: ** means $p<0.01$

According to received data, it can be concluded that the overall measurement of the six neurological scales corresponds to a change of fourteen indicators of BAP C7 and Gi4 by differential thermometry correlation between the differential thermometry BAP and the changes of neurological status, psycho-emotional state and the level of quality of life has been identified. As an important indicator, every second temperature difference between BAP and intact area of the skin can be used to assess the drug effects.

## 5 Conclusion

The indicators of BAP by differential thermometry can be criteria for evaluating the effects of drugs, which revealed the most information and reflect the process of cunctionalizing the meridian and the regulatory impacts that occur in the body during treatment. The monitoring system of action psychotropic drugs individualize the treatment of mental illness and timely track necessity to change the dosages of drugs. Using this method in clinical practice gives not only medical, but also economic effect, reducing the time of hospitalization.

The use of the developed algorithm in the treatment process of depressive states in clinical practice should optimize the treatment as well as objectify the selection of a remedy and its dosage, which is the basis for computer control systems of of medical process of mental patients.

## References

[1] Reznikov K M, Shiryaev O Y, Fedorov B A. Monitoring the action of psychotropic drugs in the treatment of schizophrenia. Human and Medicine, In: Proceedings of XVIII Russian National Congress, Moscow, Russia, 2001: 112.

[2] Mustafin A M. The connection between the biologically active points of human skin and its psychological functions. Experiment Biology and Medicine, 2003, 19(2): 30-43.

[3] Fedorov B A, Balashov D Y, Kozlov D V, et al. The device thermopuncture monitoring action of psychotropic drugs in depressive disorders. Biomedical Technology and Electronics, 2004, 10(5): 96-102.

[4] Reznikov K M, Borisova E A, Zhuravlev D V, et al. The device registration biopotentials and temperature of biologically active points: Russion. patent, 134028 U1. 2013-11-10.

[5] Lapteva V I, Borisova EA. Ability to control the effects of drugs. In: Proceedings of the VI Russian Scientific and

Practical Conference, Kazan, Russia, 2012: 86-88.
[6] Verner F A. Fundamentals of electroacupuncture. IMEDIS, Moskow, 2007: 178-201.
[7] Baranov V N. The use of microcontrollers AVR: schemes, algorithms, programs. Moskow: Dodeka-XXI, 2004: 288-341.
[8] Childs B H. Practical temperature measurement. Oxford: Oxford University Press, 2001.
[9] Fedorov B A. Development and substantiation of application method for increasing the effectiveness treatment of depressive disorders amitriptylin and tsipramil based on thermopuncture monitoring. Voronezh: Voronezh University, 2002: 24-27.
[10] Semyan A P. 500 schemes for radio amateurs, power supplies. Radio Amateur, 2005: 227-281.
[11] Shpak Y A. Programming in C language for AVR and PIC microcontrollers. Moskow: MK-Press, 2006: 400-483.
[12] Berenfus V Y, Berenfus K S, Gmyrya T P. Atlas of acupuncture points. Donetsk, 2006: 54-60.
[13] Konopelko R G. Modern technologies of drug monitoring in the treatment of schizophrenia. In: Proceedings of I8 International Conference oh New Information Technologies in Medicine, Biology, Pharmacy and Ecology: Yalta, Crimea, Ukraine, 2001: 58-59.
[14] Zhuravlev D V, Reznikov K M. Thermometry human's biologically active points. Design Radioelectronic Devices and Systems, Voronezh, Russia, 2004: 205-209.
[15] Fedorov B A. Features of termopuncture indicators in schizophrenic patients. Pressing questions of psychiatry, narcology and medical psychology, Voronezh, Russia, 2002: 130-133.
[16] Reznikov K M. Possible mechanisms of biological and pharmacological action of the anolyte and catholyte. Applied Information Aspects of Medicine, 2008, 11(2): 72-82.
[17] Nicholas J V, White D R. Traceable Temperatures. John Wiley & Sons, Chichester Ltd., 2001.
[18] Mosolov S N. Scales psychometric evaluation symptoms of schizophrenia and the concept of positive and negative disorders. Moscow: Slovo, 2001: 238-241.
[19] Brott T, Adams H P. Measurements of acute cerebral infraction: a clinical examination scale. PubMed, 2009, 20(7): 64-70.
[20] Kochetov A G. The statistical treatment of medical data: methodical recommendations for residents and postgraduate medical education, scientific workers. Moscow: RKNPK, 2012: 374-396.

# 基于穴位点体温差别的药效监测系统设计

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**摘　要：** 设计了一种通过检测生物活性点与皮肤完整区域之间温度差来监测药物疗效并优化心理疾病治疗的系统。该系统通过实时监控服药计量，以及时调整药量，从而提高治疗的有效性。系统采用两电极 Foll 方法结合中该地形解剖参考点找到生物活性点，通过 DS18B20 测量温度，利用 ATmega 32 单片机对温度进行处理并实时显示温度差，进而通过温度差反应药效。本文数据证实了温差指标 BAP C7、Gi4 与评估心理疾病严重程度的神经尺度之间的相关性。实验结果表明，温度差指标能够作为衡量药效的标准，通过监测温度差可以有效实现心理疾病药效的监测。

**关键词：** 差分测温；生物活性点；监测药效

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