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DRUG ATTITUDE AND HEALTH CONTROL BELIEFS OF PSYCHIATRIC PATIENTS

PhD thesis

László Pogány

János Szentágothai Doctoral School of Neurosciences

Semmelweis University

Supervisor: Judit Lazáry, MD, Ph.D

Official reviewers: Péter Osváth, MD, Ph.D

György Purebl, MD, Ph.D

Head of the Final Examination Committee: László Tringer, MD, D.Sc

Members of the Final Examination Committee: Szilvia Gulyás, MD, Ph.D

László Péter, MD, Ph.D

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List of abbreviations

ADDICT	subsample of patients with addictive disorders
ANOVA	Analysis of variance
BAS	Behavioral activation system
BAS Drive	Drive subscale of the Behavioral Activation System scale
BAS Fun	Fun subscale of the Behavioral Activation System scale
BIS	Behavioral inhibition system
BIS/BAS Scale	Behavioral activation/Behavioral inhibition scale
COVID-19	coronavirus disease 2019
DAI-10	Drug attitude inventory-10
Doctor HLOC	Doctor subscale of the Health Locus of Control scale
DTA	Dominant treatment attitude
F1x-F6x	ICD code groups of psychiatric disorders
GEN PSYCH	subsample of patients with general psychiatric disorders (except addictive disorders)
GLM	General linear model
HADS	Hospital Anxiety and Depression Scale
HADS-ANX	anxiety subscale of the HADS
HADS-DEP	depression subscale of the HADS
HLOC	Health locus of control
HPRS	Hong Psychological Reactance Scale
Internal HLOC	Internal Health Locus of Control
MHLC scale	Multidimensional Health Locus of Control Scale
Neg Asp	Negative aspects of medication subscale
NON-PSYCH	subsample of patients with somatic disorders
NS	non significant
PCA	principal component analysis
PHBQPT	Patient's Health Belief Questionnaire on Psychiatric Treatment
Pos Asp	Positive aspects of medication subscale
PSYCH	subsample of patients with psychiatric disorders

	(ADDICT+GEN PSYCH)
Psychol React	Psychological reactance
TMT-A	Trail making test, part A
TMT-B	Trail making test, part B
WHO	World Health Organization

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1. Introduction

1.1. The significance of adherence in the treatment of psychiatric disorders

Attitude towards drug treatment has an important influence on therapeutic outcome. The overcoming of the COVID-19 crisis is hindered by vaccine refusal despite of the proven infection of 220 million people and the death of five million worldwide, therefore this topic is of special relevance. The phenomenon sheds light on the complexity of the psychological background responsible for the refusal of a treatment with proven efficacy when fears, beliefs or mistrust may influence the decision. According to WHO data, treatment adherence of patients requiring long-term medical treatment is only about 50% in the economically developed countries [1].The insufficient adherence to treatment of psychiatric patients has been known for a long time. This issue leads to a higher number of relapses, repeated hospitalization is often needed and the course of illness may become less favourable [2]. Long lasting and frequent hospital admissions are a serious burden on the healthcare finance system and society [3]. It needs to be emphasized that the occurrence of adherence problems in the case of chronic somatic illnesses (pulmonology, cardiology, diabetology, etc.) requiring long-term medical treatment is comparable with the one encountered during the treatment of psychiatric conditions [4], however, few direct comparisons of the adherence of somatic and psychiatric patients have been performed so far.

Adherence is a multidimensional phenomenon, determined by the interplay of several factors. Some of them are related to the patient, to the medical condition requiring treatment, others are connected to the quality of patient-physician relationship, therapeutic alliance, communication, psychoeducation [5, 6], to the health care system and the social and economical factors.

In the case of psychiatric patients, the combination of educational interventions involving the patient and family members, cognitive behavior therapy, motivational interviewing and the periodic use of reinforcement techniques have proved to be useful in improving treatment adherence. Repeated sessions are required and interventions have to be performed by a trained staff in order to maintain adherence over time.[7]. Treatment adherence is negatively influenced by several patient-related factors like negative attitude towards treatment, substance abuse, poor therapeutic alliance, high

symptom intensity and unfavourable course of illness [8-10]. Cultural differences can also be responsible for poor adherence: in some countries skepticism regarding treatment, in others pharmacophobia is the most common reason of poor adherence [11]. Considering the fact that the attitude toward drug treatment is one of the important predictors of adherence [12, 13], its evaluation in the case of different patient populations is essential so that effective interventions can be planned.

Besides the attitude towards treatment, adherence is also influenced by a factor called psychological reactance, emerging as a result of the implementations of rules which endanger the freedom of personal choice, the degree of autonomy of the patient. Medication adherence can be negatively influenced by stigma, side effects, previous negative experiences, fear of addiction, and poor insight [14-16]. According to the results of a study, psychiatric patients' attitudes towards medication could be negatively influenced by a higher educational level. The results have shown that these patients were more skeptical about the usefulness of psychoactive drugs. A possible explanation of this finding is that they are more aware of the risk of dependence, the possible side effects and the fact that psychiatric drugs cannot cure mental illnesses but influence only their symptoms [17].

1.2. The concept of health control belief and health locus of control

The results of the assessment of the potential influencing factors of the complex behavior of medication taking have shown that clinical and sociodemographic factors were less powerful predictors of adherence than the beliefs regarding medication treatment. The analysis of these factors have drawn attention to the importance of beliefs regarding the impact of medication on health status [18]. Beliefs regarding health status can change during time as a result of acquired life experience [19]. Health control belief coheres with health related attitudes, emotions, coping strategies, perceived self-efficacy and perceived control.

The concept of locus of control theory was developed by Julian B. Rotter based on the social learning theory in 1954 [20]. He introduced the notion of external and internal locus of control in the mid 1960s. In the field of medical research, the relevance of the locus of control was considered for the first time during the large epidemiological

studies of tuberculosis in that decade. The theory describes the extent to which a person believes that the events are a result of his/her own actions or are rather determined by external factors, which are independent from the individual. According to the theory, a strong internal locus of control presupposes a person who believes that the majority of occurring events are the result of his/her own actions. People with external locus of control believe that events are beyond their influence and are controlled by others, external circumstances, fate or chance. The theory of locus of control was later adapted by Wallston to health related fields of research [21]. According to it, the health locus of control (HLOC) is one of the important determining factors of health behavior, and as a result, has influence on the individual's health status [22]. At the same time, health status can also influence the individual's HLOC. Studies have shown that HLOC of patients who are concomitantly suffering from more than one chronic illness is usually external.

Originally, internal HLOC was considered to be related to positive health behavior, positive emotions, while the external HLOC (control attributed to other people or chance) to have negative impact on health behavior. Early studies had shown that among people with internal HLOC the acceptance of influenza vaccination was more frequent [23], they were more informed regarding their health status than individuals with external HLOC. Patients with internal HLOC requiring treatment for tuberculosis were more motivated towards reducing the known risk factors [24].

Wallston proposed a multidimensional scale in his research on health behavior (Multidimensional Health Locus of Control Scale, MHLC scale):

1. Internal control (general internal orientation). 2. Power of others (equivalent with external control). 3. Fate or chance. Initially two questionnaires were created (versions A and B) for the MHLC scale which could be used alternatively. A version C of the questionnaire was introduced in 1994, in which the dimension „Power of others-External control" (dimension 2) was divided to the dimensions 2a. Power of doctor and 2b. Power of other people. Generally, the MHLC scale is used together with other questionnaires, and provides additional information for the complex evaluation of the results. The scale makes possible the evaluation of the locus of health control in case of different illnesses, moreover it can be adapted without major difficulties to the studied

condition. Based on the cluster analysis of the subscales, Wallston distinguished eight [21], while Rock et al. defined six different patterns [25].

Originally, the health control belief was considered to be stable over time, a component that belongs to one's personality. Later it was proved that it can be changed, moreover, the change of HLOC during the course of chronic illness is one of the necessary conditions of the patient's successful adaptation. In the case of progression or recurrence of the illness the changes in the perception of control over the situation might be essential in the process of adaptation. The degree of perceived control can increase during situations causing distress or threatening events, this can help the individual to be able to cope with the stressful situation caused by the chronic illness [26].

In an exploratory study of adherence of schizophrenic patients it was found that the patients believing that their illness could be controlled by themselves and/or by their physicians were more likely to follow their prescriptions. The connection between HLOC and adherence in this population appeared to be refined by insight [27].

Changes towards internal locus of control can be reached using psychological interventions and educational programs [28, 29]. Although it was once thought that internal and external beliefs were at opposite ends of a continuum (Rotter 1966), it is now understood that a person might simultaneously hold internal and external beliefs about the locus of control of a given phenomenon (e.g., his or her health status) [30, 31]. This might lead to the conclusion that it is not useful to focus on a single HLOC of the patient during therapeutic interventions, as the behavior of the individual in some circumstances might be influenced by a combination of different locus of control types [32].

1.3. The psychological reactance as a contributing factor in the treatment attitude

Psychological reactance is the motivational state that occurs when a behavioral freedom is eliminated or threatened with elimination. The motivational arousal has behavior-directing properties [33], targeting the re-establishment of the lost freedom. Highly reactant individuals are characterized by resistance to rules and regulations, high

desire for autonomy, high defensiveness, and low concern for social norms [34, 35]. High psychological reactance contributes to the non-adherent behavior of the patients.

Results of studies show that psychological reactance is higher in the case of more independent persons who generally rely on their own resources. People who are prone to lower psychological reactance are more likely to require assistance and to accept suggestions, advice from others [36].

The concept of psychological reactance was criticized by several authors regarding the reliability of the questionnaires which were in use for its assessment. Merz was the first to create a four factor instrument of 18 items called Psychological Reactance in 1983 [37]. Later, the Hong Psychological Reactance Scale was developed [38], which has become a widely used instrument in many countries despite of the fact that in certain studies its internal consistency has proved to be weak. The HPRS has been criticized due to its proneness to reflect higher psychological reactance in the case of men and younger subjects than in women or elderly population. However, psychological reactance is one of the influencing factors of attitude towards treatment, thus, 3 items of the HPRS were selected by De las Cuevas et al for the PHBQPT [39].

1.4. The Patient's Health Belief Questionnaire on Psychiatric Treatment (PHBQPT)

Patient's Health Belief Questionnaire on Psychiatric Treatment (PHBQPT) is an instrument developed in 2019 by De las Cuevas and colleagues which makes possible a thorough assessment of health locus of control, of attitude towards drug treatment and of the psychological reactance [39]. The 17 items of the PHBQPT scale are grouped in 5 subscales: Positive Aspects of Medications (PosAsp); Negative Aspects of Medications (NegAsp); control over health attributed to physician (Doctor HLOC), health attributed to one's own actions (Internal HLOC) and psychological reactance (PsycholReact). The 17 item PHBQPT was compiled from the Drug Attitude Inventory (DAI-10) [40], the MHLC Form C [30] and HPRS scales [41] (total number of items of the three scales is 42). The PHBQPT can be completed in 15 minutes in contrast with the 1.5 hours completion time of the initial questionnaires. For this reason, the clinical usability of the instrument has increased considerably. Its repeated completion during the treatment makes possible the monitoring of treatment-emergent changes of these factors and

identification of the objectives of interventions. Using the questionnaire, the physician can assess the patient's feelings, attitude towards drug treatment, the locus of health control, one's sense of responsibility for his/her own health status.

1.5. Motivational factors in the treatment attitude

The behavior of the patient towards treatment is influenced by an affective-motivational regulation system, the direction of the action is determined by the dynamic balance of the appetitive and aversive behavior. Jeffrey Gray's Reinforcement Sensitivity Theory [42, 43] describes the individual differences of human personality structure based on animal research results of learning theory. The original theory is based on the concept that behavior is driven by two distinct motivational systems (Behavioral Inhibition System, BIS and Behavioral Activation System, BAS). Behavioral Activation System activates when unconditioned reward or relief from punishment can be expected. In such circumstances BAS facilitates the approach behavior. High BAS engagement can be observed in addictions, in the background of impulsivity and hostile behavior, while low BAS engagement may lead to depression [44].

BIS is responsible for organizing behavior in the presence of aversive stimuli, when punishment or no reward can be expected [45]. BIS can interrupt the ongoing behavior and increase the level of arousal and attention so that a new, adaptive behavior can be rapidly planned and started as a response to the threatening circumstances. BIS compares the most probable outcome which can be expected with the present situation and if needed, halts the ongoing behavior in order to trigger a more appropriate behavior. High BIS sensitivity leads to proneness to rumination and concern as personality traits, the individual is detecting and analyzing continuously the aversive stimuli of the environment, which may result in generalized anxiety or obsessive-compulsive disorder. The emerging psychopathology is the result of insufficient conflict-resolving capacity of the system, the behavior cannot be adapted properly to the environmental factors [46]. High BAS sensitivity drives the behavior towards attaining the desired goal, the characteristic personality traits are optimism, reward sensitivity and impulsivity. According to the BIS/BAS model, there are distinct neuroanatomical

structures in the background of all of its components, which are responsible for identifying, analyzing the environmental stimuli and the planning of the most adaptive behavior. As a response to the different types of environmental stimuli, different neural structures are activated which results in different emotional states, motivational and behavioral responses [46]. The Behavioral Inhibiton System and Behavioral Activation System Scale (BIS/BAS Scale) is a widely used tool based on Gray's Reinforcement Sensitivity Theory which proved to be appropriate for assessing the sensitivity of the behavioral activation and inhibition systems [47]. The BIS/BAS questionnaire comprises 24 items which can be rated on a four point Likert scale by the patient. The items are grouped in four factors, respectively the BIS (7 items referring to the reactions emerging related to the expected punishment) and three BAS scales: BAS-Fun (5 items), BAS-Drive (4 items) and Reward Responsiveness (5 items). Besides these, the questionnaire comprises four filler items (1, 6, 11, 17). In spite of the low number of items, the internal validity of the four scales proved to be satisfactory and the tool proved to be stable in time as well. The questionnaire was adapted and validated to Hungarian sample [48].

1.6. Affective-emotional factors in health behavior

According to Gray's theory, the interindividual differences of personality can be explained by the sensitivity differences of the neural structures. The characteristic emotional state, motivational direction, impulsivity, the level of anxiety of each individual are the result of the difference of activation pattern of the neural structures [42, 43]. In other words, according to this model, behavior is influenced by the sensitivity of specific neurobiological structures and the learning process based on data resulting from the continuous interaction between the environment and individual, which emphasizes that it cannot be ignored in studies of the attitude towards treatment. As it was mentioned earlier, attitude towards treatment is influenced by the affective state, the intensity of affective symptoms. Regardless of the condition requiring treatment, anxiety and depressive symptoms are the most frequent concomitant symptoms in the case of psychiatric inpatients. Considering this, it is reasonable to evaluate the impact of affective symptoms on the attitude towards treatment of the

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patients. In our research, we intended to assess besides the attitude towards treatment, psychological reactance and health control belief also the affective-motivational factors which influence treatment adherence, and to identify correlations between variables and compare the characteristics of different diagnostic groups.

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2. Objectives

The following research objectives have been determined:

I. Validating analysis of the Hungarian version of the PHBQPT questionnaire in a sample of psychiatric patients.

a. The translation and adaptation of the questionnaire to Hungarian.

b. The comparison of the per item and subscale mean scores of the Hungarian sample with the ones published by the developers of the scale.

c. The structural and factor analysis of data obtained by using the Hungarian version of the questionnaire.

II. Exploration of the interaction matrix of PHBQPT subscales, the affective symptoms and the behavioral inhibition/behavioral activation system scale.

III. Analysis of the pattern of treatment attitudes, the multiple carriers and the carriers of DTAs in the sample of psychiatric patients.

IV. Assessment of the distribution of treatment attitude subtypes identified with the PHBQPT questionnaire in samples of psychiatric and non-psychiatric patients.

V. Assessment of the distribution of treatment attitude subtypes identified with the PHBQPT questionnaire in different diagnostic subgroups of psychiatric patients.

VI. Determining the change of the attitude towards treatment as a result of relevant therapy and analysis of associations between change of treatment attitude, change of affective symptoms and cognitive improvement.

3. Results

3.1. The validation and analysis of the Patient's Health Belief Questionnaire on Psychiatric Treatment in a sample of Hungarian psychiatric patients

3.1.1. Analysis of the total scale

The data of 188 patients (115 women and 73 men, mean age 32.8±10.7 year) with psychiatric disorders were analysed in this study. The means of single items and comparison of the originally published values are presented in Table 1. Single item mean was 4.17 (minimum=3.01; maximum=5.48; variance=0.37) and mean of single item variance was 1.85 (minimum=0.75; maximum=2.48; variance=0.21). The internal consistency of the whole scale is acceptable (Cronbach's alpha=0.62). If any item was deleted, the Cronbach's alpha of scale has not improved significantly. Using principle component analysis yielded 5 factors corresponding to 5 subscales of the scale. While one factor model showed 26.4% of explained variance, in case of 5 factor model it is 60.8%. Thus, the factorial analysis confirmed the validity of 5 subscale structure in our sample. The correlation matrix of the subscales resulted in similar values as the original description of the scale (Table 2). Effects of gender were not significant on either subscales (p>0.05 in all cases).

Table 1 Mean scores of items in our study population and comparison with values published by De las Cuevas et al. (2019) [39] [49]

PHBQPT items	**Means±S.D.**	**De las Cuevas (2019)**
(1) I am directly responsible for my condition getting better or worse.	4.7±1.3	4.7±1.7
(2) If I see my doctor regularly, I am less likely to have problems with my condition.	4.5±1.4	4.6±1.7
(3) When someone forces me to do something, I feel like doing the opposite**.**	3.0±1.5	2.7±1.8

(4) For me, the good things about medication outweigh the bad.	4.3±1.4	4.6±1.7
(5) I feel strange, "doped up", on medication.	3.5±1.4	3.1±2.0
(6) The main thing which affects my condition is what I myself do.	4.4±1.3	4.2±1.8
(7) Following doctor's orders to the letter is the best way to keep my condition from getting any worse **.**	5.1±1.0	4.9±1.5
(8) I resist the attempts of others to influence me.	4.3±1.4	3.3±1.9
(9) Medications make me feel more relaxed.	4.3±1.3	4.9±1.7
(10) Medication makes me feel tired and sluggish.	3.7±1.5	3.7±2.0
(11) I feel more normal on medication.	4.1±1.4	4.3±1.8
(12) If my condition takes a turn for the worse, it is because I have not been taking proper care of myself.	3.9±1.5	4.2±1.9
(13) Whenever my condition worsens, I should consult a medically trained professional.	5.5±0.9	5.5±1.2
(14) It is unnatural for my mind and body to be controlled by medications.	3.5±1.6	2.9±1.9
(15) My thoughts are clearer on medication.	3.6±1.6	4.0±1.9
(16) Taking medication will prevent me from having a breakdown.	4.1±1.3	4.1±1.9
(17) I become angry when my freedom of choice is restricted.	4.1±1.4	4.2±1.8

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Subscales		
Positive Aspects of Medications	20.3±5.6	18.1±4.8
Negative Aspects of Medications	10.6±3.7	9.7±4.2
Doctor HLOC	15.1±2.7	15.1±3.4
Internal HLOC	12.9±3.2	12.9±4.2
Psychological Reactance	11.3±2.8	10.2±3.8

Table 2 Pearson's correlation test of subscales of the PHBQT [49]

**<p 0,01 Numbers in the brackets refer to the R values published by De las Cuevas et al 2019 [39]

	NegAsp	**DoctorHLOC**	**InternalHLOC**	**PsychReact**
PosAsp	-0.32**	0.41**	0.21**	0.09
	(-0.19)	(0.38)	(0.20)	(-0.015)
NegAsp	-	-0.31**	-0.10	0.07
		(-0.10)	(-0.19)	(0.22)
Doctor HLOC	-	-	0.34**	0.08
			(0.22)	(-0.12)
Internal HLOC	-	-	-	0.11
				(0.09)

3.1.2. Analysis of the subscales

The distributions of the scores of subscales are deviated from normality based on the Kolmogorov-Smirnov test in all cases ($p<0.05$ in all cases).

In the PosAsp subscale the mean of single items is 4.08 and the variance is 1.98. The internal consistency of the subscale is considerably strong (0.82) and the correlations of items within subscale also indicated tight relationships. The strongest relationship can be observed between item 15 and 11, while the weakest between 16 and 4. The internal consistency of the NegAsp subscale is 0.72, while the mean of single item is 3.57 and the variance is 2.25. The items showed strong correlation, the weakest relationship can be observed between item 14 and 10, while the strongest correlation between 10 and 5.

The Cronbach's alpha of the Doctor HLOC is 0.65. The mean of single items is 5.04 and the variance is 1.24. The correlations among items are weaker than the first two subscales, namely the R values are under 0.5. Analysing the connections between the Doctor HLOC subscales and the whole scale and other factors, we found that the most predictive components are Internal HLOC and age.

In the case of the Internal HLOC subscale the Cronbach's alpha is 0.68. The mean of single item is 4.32 and the variance is 1.83. All three items showed correlations characterized with R values less than 0.5. The strongest relationships were found with Doctor HLOC and PsychReactance.

The internal consistency of the PsycholReact subscale is weak (Cronbach's alpha=0.25). The mean of single item is 3.81 and the variance is 2.04. The correlations between items indicated weak relationships and the R values of all three items were less than 0.2. Only the Internal HLOC subscale had predictive effect on this scale.

3.2. Patients' control beliefs, motivations and current affective symptoms in association with the psychiatric treatment

3.2.1. Descriptive statistics

The data of 295 inpatients (162 women and 133 men, mean age was 45.9±14.8 year) treated with psychiatric disorder were analysed in this study. The mean scores of the phenotypic scale scores of the total sample and by gender distribution are presented in Table 3.

Table 3 Mean scores of the subscales in the total sample and in men and women separately [50]

	Total sample	**Men**	**Women**
Positive Aspect	20.3±5.6	20.6±5.7	20.2±5.6
Negative Aspect	10.6±3.7	10.4±3.5	10.7±3.8
Doctor HLOC	15.0±2.9	15.1±3.8	15.0±2.9
Internal HLOC	13.1±3.3	13.0±3.3	13.3±3.2
Psychological Reactance	11.4±2.7	11.3±2.8	11.5±2.6
HADS-ANX	9.8±4.9	9.5±4.4	9.9±5.1
HADS-DEP	7.7±5.4	7.2±5.0	8.1±5.6
BIS	20.7±3.9	19.8±3.7[a]	21.2±3.9[a]
BAS total	36.6±7.4	37.9±6.8	35.7±7.6
BAS Drive	10.6±2.9	10.9±2.7	10.3±3.1
BAS Fun seeking	10.3±2.7	10.9±2.5[b]	9.9±2.5[b]
BAS Reward Responsiveness	15.7±2.9	16.0±2.7	15.4±3.1

a p=0.02; b p=0.02

HADS-DEP, Depression subscale of the Hospital Anxiety Depression scale; HADS-ANX, Anxiety subscale of the Hospital Anxiety Depression scale; BIS, Behavioral Inhibiton System scale; BAS, Behavioral Activation System scale.

3.2.2. Analysis of the prevalence and the structure of dominant treatment attitudes

We introduced a new variable using the cut-off point by mean in all subscales of the PHBQPT and we named it as dominant treatment attitude (DTA; $DTA_{Positive\ Aspect}$ =0, if <20.3 and it is= 1, if >20.3; $DTA_{Negative\ Aspect}$ =0, if <10.6 and it is = 1, if >10.6;

$DTA_{Doctor\ HLOC}$ =0, if it is <15; and it is= 1 if >15.0; $DTA_{Internal\ HLOC}$ = 0, if <13.1 and it is= 1, if >13.1 and $DTA_{Psychological\ Reactance}$ =0, if <11.4 and it is =1 if >11.4 score). The frequency of the DTA is relatively high, since the different types of DTA-s are present in more than 90% of the sample. The different types of DTA-s associated with subscales of the PHBQPT are presented on Figure 1. In case of 4 subscales, the DTA occurred in approximately half of the population, the presence of $DTA_{PsycholReact}$ is only 14.5%. The most common DTA has been shown to be the Doctor HLOC.

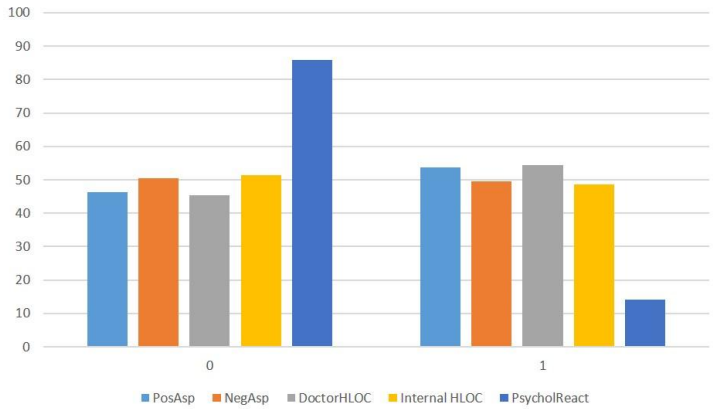

Figure 1 Prevalences of dominant treatment attitudes of different PHBQPT subscales [50]

0=no dominant treatment attitude; 1=scores of the subscales have reached the limit of dominant category

3.2.3. Quantitative and qualitative analysis of multiple DTA prevalence

With regard to the fact that the PHBQPT subscales are meant to describe the complexity of the factors influencing drug adherence, in spite of the dichotomous nature (Negative Aspect-Positive Aspect; Doctor HLOC-Internal HLOC), the subscales do not exclude each other, but the different components provide a more detailed picture. Accordingly, the maximal score can be attained on more subscales concomitantly, which reflects the complexity of patients' attitude toward treatment and gives rise to further analysis. In order to analyze the variations of the concomitantly occurring DTA-s, we assessed the occurrence frequency of the different DTA carriers. As it is shown on

Figure 2, 6.4% of the sample is not DTA carrier, 21% is single DTA carrier, 33 % is double DTA carrier, 26 % carries 3, 11% carries 4 and 2% carries 5 DTA-s (Figure2).

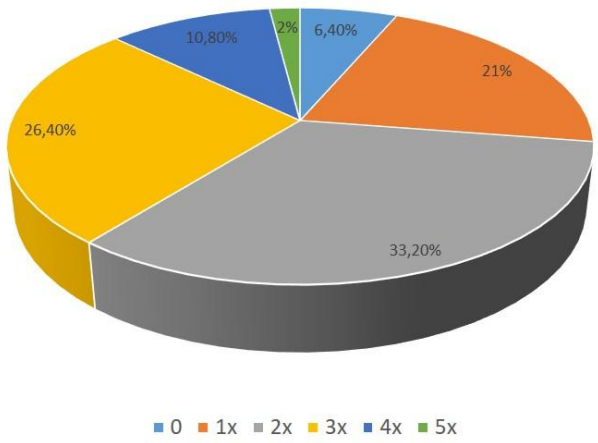

Figure 2 Prevalences of non-carriers and carriers of different number of DTA-s in the study sample [50]

0=patients with no dominant treatment attitude (DTA); 1x=patients with one DTA; 2x=patients with two (double) DTAs; 3x=patients with three DTAs; 4x=patients with four DTAs; 5x=patients with five DTAs.

Since the double DTA occurred most frequently in the sample, we analyzed the ratio of occurrence of the possible pairs (Table 4; Figure 3). According to our results, the most frequent pairs were the PosAsp+Doctor HLOC (37%) and the Internal HLOC+Doctor HLOC (33%). These pairs were followed by the PosAsp+Internal HLOC (29%), the NegAsp+Internal HLOC (24%), the NegAsp+Doctor HLOC (23%) and the NegAsp+PosAsp (21%). The pairs with Psychol React were the least frequent ones in the sample (7-8%).

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Table 4 Distribution of double DTA carriers with different DTA patterns [50]

	PosAsp	**NegAsp**	**DoctorHLOC**	**Internal HLOC**
PosAsp				
NegAsp	61(20.6%)			
DoctorHLOC	108(36.5%)	68(23.0%)		
InternalHLOC	85(28.7%)	70(23.6%)	100(33.0%)	
PsycholReact	24(8.1%)	22(7.4%)	23(7.8%)	23(7.8%)

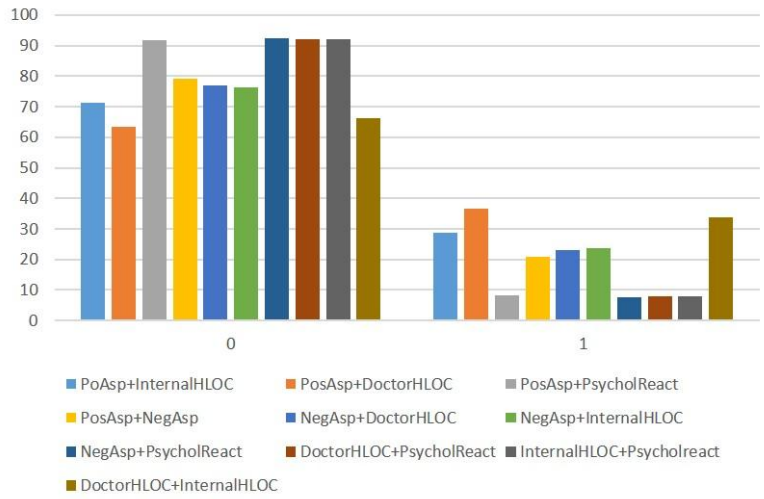

Figure 3 Frequencies of the different types of double DTAs in the study sample of psychiatric inpatients [50]

0=no DTA; 1=double DTA

We assessed the presence of a significant correlation between the DTA pairs, the BIS/BAS scores and the HADS anxiety and depression subscores (Table 5). A marginally significant correlation could be found between the PosAsp+Internal HLOC and the HADS-DEP score. The carriers of this DTA reached a lower score on the

depression subscale of the HADS than the non-carriers ($p=0.07$). The BAS Drive subscale score was higher in those pairs in which the Psychol React was present. Besides this, the carriers of Doctor HLOC+Psychol React pair scored higher on the BAS Fun seeking subscale and their BAS total score was higher as well compared to the non-carriers ($p=0.02$; $p=0.003$). The Doctor HLOC+Internal HLOC pair separated most sharply the sample regarding the anxiety and depression subscale scores. The HADS-ANX and HADS-DEP scores of the carriers of this double DTA were significantly lower ($p<0.001$ in both cases). While the BIS score was significantly lower ($p=0.04$), the BAS total score was higher. Only one of the BAS subscales, the BAS Fun seeking did not show any significant relatedness.

Table 5 Means and S.D. values of the phenotypic scale scores of different types of double DTA carrying [50]

		HADS-ANX	HADS-DEP	BIS	BAS Drive	BAS Fun seeking	BAS Reward Resp	BAS total
PosAsp+DoctorHLOC	0	9.9±4.7	7.9±5.2	20.9±3.9	10.3±3.0	10.4±2.7	15.3±3.0	36.0±7.7
	1	9.5±5.1	7.4±5.6	20.3±3.7	11.0±2.9	10.3±2.6	16.1±2.8	37.4±6.8
PosAsp+InternalHLOC	0	10.2±4.9	8.2±5.3	20.8±3.9	10.4±3.0	10.4±2.7	15.5±2.9	36.3±7.5
	1	8.7±4.7	6.6±5.5	20.3±3.8	11.1±2.9	10.1±2.7	16.1±2.9	37.3±7.1
PosAsp+PsycholReact	0	9.6±4.8	7.6±5.4	20.7±3.8	10.4±2.9[a]	10.2±2.6	15.6±2.9	36.2±7.1
	1	10.9±5.3	8.8±5.2	20.8±4.4	11.8±2.8[a]	11.3±3.2	15.9±3.8	39.0±8.8
PosAsp+NegAsp	0	9.6±4.9	7.6±5.4	20.8±3.9	10.5±2.9	10.2±2.7	15.5±2.9	36.2±7.3
	1	10.3±4.5	8.2±5.1	20.3±3.8	11.2±3.2	10.6±2.8	16.2±3.3	38.0±7.8
NegAsp+Doctor	0	9.8±4.9	7.8±5.4	20.9±3.9	10.6±3.0	10.3±2.7	15.5±3.0	36.4±7.6
	1	9.5±4.8	7.5±5.5	19.7±3.8	10.5±2.9	10.4±2.7	16.1±2.8	36.9±6.8
NegAsp+InternalHLOC	0	9.8±4.9	8.1±5.5	20.9±3.9	10.4±3.1	10.1±2.6	15.4±2.9	35.9±7.4
	1	9.6±4.9	6.7±5.0	19.8±3.5	11.1±2.8	10.8±2.9	16.2±3.0	38.1±7.0
NegAsp+PsycholReact	0	9.7±4.8	7.9±5.4	20.7±4.0	10.4±2.9[b]	10.2±2.7	15.6±3.0	36.2±7.3
	1	10.2±5.5	6.8±5.0	20.4±3.1	12.1±2.5[b]	11.2±2.9	16.1±2.8	39.4±7.5
DoctorHLOC+PsycholReact	0	9.8±4.8	7.9±5.4	20.7±3.9	10.3±2.9[c]	10.1±2.7[d]	15.5±3.0	35.9±7.3[e]
	1	9.6±5.4	6.3±5.6	20.5±3.6	12.7±2.6[c]	11.6±2.5[d]	16.6±2.4	40.9±6.2[e]
Internal+PsycholReact	0	9.9±4.8	7.9±5.3	20.8±4.0	10.3±2.9[f]	10.2±2.7	15.6±2.9	36.2±7.2
	1	8.9±5.0	6.1±5.4	19.6±2.7	12.6±2.7[f]	11.0±2.9	15.8±3.2	39.4±8.0
DoctorHLOC+InternalHLOC	0	10.8±4.7[g]	9.1±5.0[h]	21.2±3.9[i]	10.1±3.0[j]	10.3±2.9	15.1±3.1[k]	35.4±7.9[l]
	1	8.1±4.7[g]	5.6±5.3[h]	19.9±3.8[i]	11.4±2.7[j]	10.4±2.4	16.4±2.6[k]	38.2±6.2[l]

Differences between the mean scores were significant at a, p=0.04; b, p=0.01; c, p<0.001; d, p=0.02; e, p=0.003; f, p=0.001; g, p<0.001; h, p<0.001 i, p=0.04; j, p=0.003; k, p=0.005;l p=0.01 by GLM tests

3.2.4. Association analysis of PHBQPT subscales and BIS/BAS and HADS

A correlation could be found between Pos Asp and BAS Reward Responsiveness (p=0.04) and Neg Asp and BAS Fun seeking (p=0.05) subscales. Doctor HLOC correlated with BAS Fun seeking (p=0.01) and with BAS Reward Responsiveness (p=0.008), while Internal HLOC correlated only with BAS drive (p=0.002; Table 6). Psychol React correlated with BAS Drive as well (p=0.005). It can be observed that Positive Aspect and Doctor HLOC differs from the other factors through the higher score of Reward Responsiveness, while Internal HLOC and Psychol React through the higher BAS Drive (Table 6). Regarding the general affective symptoms, it was found that with lower HADS-DEP score correlated higher Doctor HLOC (p=0.02), high Internal HLOC (Table 6; p=0.007) and high Psychological Reactance scores (p=0.0002), all these DTA-s were of protective value against depressive symptoms (Table 6). Interestingly, higher Psychological Reactance scores were of protective value against depressive symptomatology (p=0.0002) but potentiated anxiety (p=0.0004) (Table 6).

The BIS/BAS subscale scores correlated with the HADS scores in a manner that is in conformity with data found in already published sources (Table 6). Higher BIS scores correlated significantly with more intense anxiety, while all BAS subscale scores were lower in case of intense anxiety with the exception of BAS Reward Responsiveness. HADS depression scores were higher in the case of high BIS subscores and lower BAS subscale scores could be observed when HADS-DEP scores were higher. An important difference could be observed between anxiety and depressive symptoms, namely, only depressive symptoms correlated with Reward Responsiveness, anxiety did not.

Table 6 Results of the GLM tests of the PHBQPT, the BIS/BAS and the HADS subscales [50]

	PosAsp	**NegAsp**	**Doctor HLOC**	**Internal HLOC**	**Psychol Reactance**	**HADS-ANX**	**HADS-DEP**
HADS-ANX	NS	NS	NS	NS	0.0004		
HADS-DEP	NS	NS	0.02	0.007	0.0002		
BIS	NS	NS	NS	NS	NS	$1.5x10^{-8}$	$6.7x10^{-7}$
BAS total	NS	NS	NS	NS	0.01	NS	$1.2x10^{-8}$
BAS Drive	NS	NS	NS	0.002	0.005	0.001	$8.0x10^{-8}$
BAS Fun seeking	NS	NS	0.01	NS	NS	0.006	0.003
BAS RewardResp	0.04	NS	0.008	NS	NS	NS	0.002

HADS-DEP, Depression subscale of Hospital Anxiety Depression scale; HADS-ANX, Anxiety subscale of Hospital Anxiety Depression scale; BIS, Behavioral Inhibiton System scale; BAS, Behavioral Activation System scale.

3.2.5. Differences in the PHBQPT, BIS/BAS and HADS scale scores in different diagnostic categories

We analyzed the difference between diagnostical categories regarding the scores of the phenotype questionnaire. Our results did not show major differences between the groups, with the exception of Doctor HLOC and BAS Fun seeking. The analysis has shown that the Doctor HLOC score of psychotic patients was lower than the score of the affective group (p=0.002). Besides this, the score of BAS Fun seeking scale was higher in the case of patients with personality disorders than of the patients treated for affective disorders (p=0.008; Table 7).

Table 7 Differences of PHBQPT and BIS/BAS scale scores in different diagnostic categories [50]

	F2x	F3x+F4x	F6x	Sig
PosAsp	19.8±0.5	21.1±0.6	19.9±5,0	NS
NegAsp	10.9±4.3	10.2±3.2	10.3±2.9	NS
Doctor HLOC	14.4±3.4	15.6±2.3	15.3±2.2	0.002 (F2 vs F3+F4)
Internal HLOC	13.0±3.4	13.1±2.8	13.8±2.8	NS
Psychol React	11.6±2.8	11.2±2.7	12.0±2.7	NS
BIS	20.2±3.7	21.2±4.1	20.9±4.2	NS
BAS Drive	10.7±3.2	10.4±2.9	10.9±2.6	NS
BAS Fun seeking	10.4±2.8	9.9±2.6	11.6±2.5	0.008 (F3+F4 vs F6)
BAS total	36.6±7.5	35.7±7.5	39.0±6.7	NS

Results of ANOVA tests and Tukey's post hoc tests are presented.

F2x=ICD code of group of psychotic disorders; F3x=ICD code of group of affective disorders; F4x=ICD code of anxiety disorders; F6x=ICD code of group of personality disorders. F3x and F4x were included in one group for statistical analysis because of the low number of patients and the frequent co-occurrence of these diagnoses.

3.3. Health control belief and attitude toward treatment in psychiatric and non-psychiatric clinical samples

3.3.1. Descriptive statistics

The data of 189 patients (GEN PSY=106; ADDICT=42; NON PSY=41) were analysed in this study. Gender ratio was equilibrated in the PSYCH subsample (GEN PSYCH+ADDICT), but women were overrepresented in the NON-PSYCH sample (p=0.012). The effect of age and gender were tested by general linear models on the PHBQPT subscales. We found that in the NON-PSYCH sample only Psychological Reactance depended on the gender (p=0.045). However, age had significant effect on Doctor HLOC subscale in GEN PSYCH+ADDICT subsamples (p=0.025; p=0.023;

respectively). Interestingly, Internal HLOC was gender-dependent only in the ADDICT subgroup (p=0.026). The detailed results of descriptive statistical analyses are shown in Table 8.

Table 8 Mean age and gender prevalences in the investigated subsamples [51]

	N	Age (mean±S.D.)	Gender (male/female)
PSYCH (1)	148	46.7±14.7	74/74
GEN PSYCH (2)	106	48.0±15.6	48/58
ADDICT (3)	42	43.2±11.8	28/14
NON-PSYCH (4)	41	66.8±13.5	11/30
p-value		(1) vs. (4) <0.001	(1) vs. (4) 0.012

Differences between groups were calculated by t-test and chi square tests.
PSYCH sample=GEN PSYCH+ADDICT subgroups

3.3.2. Comparison of PHBQPT scores in the GEN PSYCH and NON-PSYCH clinical subsamples

In this analysis the highest degree of agreement was found at the item „Whenever my condition worsens, I should consult a medically trained professional" in both subsamples (5.3±1.1 and 5.6±0.7; p>0.05), similarly as in the case of the results of the study of De las Cuevas et al (2019) [39]. However, psychiatric patients considered significantly less important to follow their physician's suggestions (5.1±1.0 vs 5.5±0.8; p=0.03) and found the regular visits to their doctors to be less effective (4.6±1.4 vs 5.2±1.1; p=0.010). Surprisingly, resistance against the influence of others was more pronounced among patients with somatic disorders than in the PSYCH subgroup (4.3±1.4 vs 5.0±1.6; p =0.01). Concerning the PHBQPT subscales, NON-PSYCH participants scored significantly higher on DOCTOR HLOC subscale compared to GEN PSYCH group (15.3±2.7 vs 15.9±2.7; p=0.04). There was no significant difference between the two subgroups concerning the drug attitude subscales.

3.3.3. Comparison of PHBQPT scores in the GEN PSYCH and ADDICT clinical subsamples

As it was expected, participants treated for an addiction gave significantly different responses on almost all items of the questionnaire. Patients with addictions scored significantly higher on items 1, 2, 3, 6, 7, 8, 12 and 14 (all *p*-values <0.05). In contrast, robustly higher scores were given by GEN PSYCH subgroup members on items 4, 11, 15 and 16 (all *p*-values <0.05). Significantly higher scores on Positive Aspects of the medication subscale were found in the GEN PSYCH subpopulation while there was no difference in Negative Aspect between the two subsamples. However, patients with addictions scored significantly higher on Doctor HLOC, Internal HLOC and Psychological Reactance subscales (all *p*-values<0.05). Patients with addictions scored higher on Doctor HLOC subscale than patients with psychotic (F2) and affective (F3) disorders. Furthermore, patients with addictive disorders also scored higher on Internal HLOC subscale compared to the subjects with psychotic (F2), affective (F3) and anxiety (F4) disorders (Figure 4).

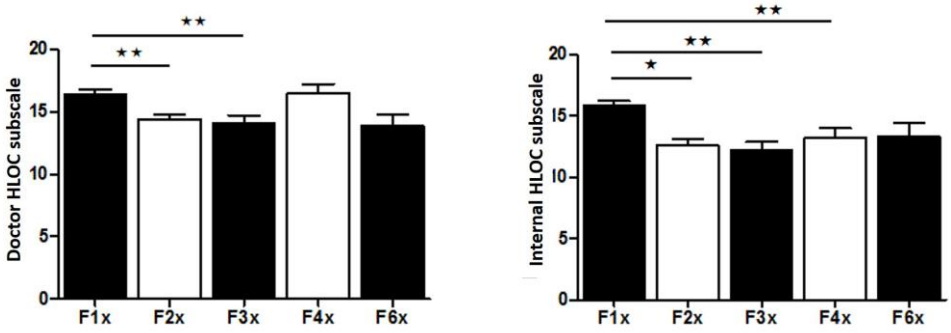

Figure 4 Significant differences of Doctor HLOC and Internal HLOC subscale scores among the diagnostic categories [52].

Differences between diagnostic groups were analyzed with ANOVA and Tukey's post hoc tests.

*p<0.05; **p<0.005

F1= ICD code of group of addictive disorders; F2=ICD code of group of psychotic disorders; F3=ICD code of group of affective disorders; F4=ICD code of anxiety disorders; F6=ICD code of group of personality disorders.

3.3.4. Comparison of the three clinical subgroups

Regarding the associations of mean scores of PHBQPT subscales among the three clinical samples, we found that Positive Aspect score was significantly higher in the GEN PSYCH than in the ADDICT (*p*ANOVA= 0.004); Doctor HLOC score was lower in the GEN PSYCH compared to the ADDICT and to the NON-PSYCH (*p*ANOVA= 0.002 and 0.04, respectively); Internal HLOC score was higher compared to the GEN PSYCH (*p*ANOVA= $8x10^{-7}$), and Psychological Reactance score was higher in the ADDICT compared to the GEN PSYCH (*p*ANOVA= 0.04) (Figure 5).

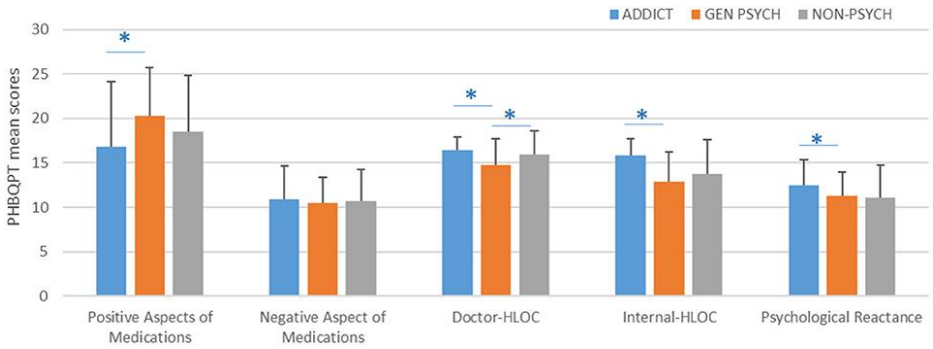

Figure 5 Significant differences of PHBQPT subscale scores among the psychiatric, non-psychiatric and addiction subgroups [51].

Differences between diagnostic groups were analyzed with ANOVA and Tukey's post hoc tests. *p<0.05

3.4. Analysis of the change of treatment attitude after pharmacological treatment

The baseline and follow-up after a 14-day treatment data of 84 patients with psychiatric disorders were analysed in this study. The Negative Aspect subscale score at

the baseline showed a significant correlation with the HADS-ANX score (p=0.015). The Negative Aspect score decreased significantly (p=0.001), while Doctor HLOC (p=0.001) and Internal HLOC subscale scores increased significantly during the two-week treatment period. In the case of neurocognitive tests, the time required to perform the TMT-A (p=0.001) and the TMT-B (p=0.002) decreased as well. The speed of performance of the Stroop test increased, the time needed to perform the tasks became shorter ($p_{Stroop1}$=0.004; $p_{Stroop3}$=0.034) and the number of errors was lower at $visit_2$ compared to $visit_1$ ($p_{Stroop3}$=0.044). However, there was no difference between the two visits regarding the number of errors at the first task and at the second task, neither the time, nor the number of errors changed significantly (Table 9).

According to the results of the GLM tests, there was a strong correlation between the decreasing NegAsp subscale scores and the decrease of the HADS-ANX (p=0.002) and HADS-DEP scores (p=0.006) as well. Besides these, correlation could be found between the increasing scores of the PosAsp subscale and the decrease of HADS-DEP (p=0.028) (Table 10). No correlation could be found between the improvement of neurocognitive functioning and the changes of scores related to the attitude towards drug treatment. No significant influencing effect of age and sex on attitude towards drug treatment could be found.

Table 9 Mean scores of PHBQPT subscales, HADS and neurocognitive tests at the $visit_1$ and $visit_2$ [53].

	$Visit_1$	**$Visit_2$**	**Sig.***
Positive aspect	20.04±6.2	20.45±6.05	NS
Negative aspect	11.02±4.03	9.64±3.68	0.001
Doctor HLOC	14.78±3.16	16.09±2.47	0.001
Internal HLOC	13.13±3.42	14.13±3.07	0.006
Psychol React	11.60±2.89	11.49±3.07	NS
HADS ANX	10.15±4.95	9.69±5.34	0.002
HADS DEP	7.99±5.52	7.58±5.13	NS
TMT-A time	49.31±20.53	40.31±19.03	0.001
TMT-B time	134.28±84.79	94.03±64.12	0.002
Stroop T1	60.06±20.53	51.83±15.42	0.004

Stroop T2	80.83±33.24	74.46±23.26	NS
Stroop T3	143.69±73.58	122.86±45.43	0.034
Stroop E1	2.86±12.68	0.03±0.17	NS
Stroop E2	4.54±19.32	0.77±1.21	NS
Stroop E3	3.85±5.91	2.09±2.31	0.044

*p-value of the paired sample t-tests

Table 10 Associations of the delta values of the scores of PHBQPT subscales, HADS scores and neurocognitive tests [53].

	Δ PosAsp	**Δ NegAsp**	**Δ Doctor HLOC**	**Δ Internal HLOC**	**Δ Psychol React**
Δ HADS- ANX	NS	0.002	NS	NS	NS
Δ HADS –DEP	0.028	0.006	NS	NS	NS
Δ TMT-A	NS	NS	NS	NS	NS
Δ TMT-B	NS	NS	NS	NS	NS
Δ Stroop T1	NS	NS	0.012	NS	NS
Δ Stroop T2	NS	NS	NS	NS	NS
Δ Stroop T3	NS	NS	NS	NS	NS
Δ Stroop E1	NS	NS	NS	NS	NS
Δ Stroop E2	NS	NS	NS	0.038	NS
Δ Stroop E3	NS	NS	NS	NS	NS

p-values of the GLM tests are presented. Stroop T, time; Stroop E, error.

4. Discussion

4.1. Validation and analysis of the Hungarian version of the PHBQPT

In our study we performed an analysis of the Hungarian version of the Patient's Health Belief Questionnaire on Psychiatric Treatment (PHBQPT). As the assessment of internal consistency and factorial analysis of the scale was not included in the original paper on the PHBQPT, this is the first structural analysis of the instrument. Validity, reliability and the factorial structure of the scale are acceptable and suitable for the clinical assessment of health control belief and drug attitude. The variance of subscales was independent of age and gender. According to the results of our study, this instrument can be used in a Hungarian sample of psychiatric patients.

De las Cuevas et al published the results of their study on the PHBQPT in 2019. They enrolled 588 ambulatory care psychiatric patients [39]. The authors selected from the items of MHLC, DAI-10 and HPRS the most relevant ones considering the weighting factor and impact of each item on the total score of the source scale and determined the item's predictive value regarding adherence. Our results have shown that the internal consistency of the subscales is acceptable with the exception of the Psychological reactance subscale, which is a short subscale comprised of three items with a particularly weak consistency (Cronbach's alpha =0.21). However, the factorial analysis supported the criteria of separation and uniformity of the 5 subscales. In the original study, the highest mean score (5.5±1.2) could be observed at item 13 „Whenever my condition worsens, I should consult a medically trained professional", similarly, in our study this item was given the highest score by the patients (5.5±0.9). The scores given at almost all items showed similarity in our sample with the item scores presented by the authors of the original scale.

On the other hand, there were higher differences between the mean scores of our sample and of the original analysis at the following three items: item 9 "Medications make me feel more relaxed" (our study: 4.3±1.3 vs original study: 4.9±1.7); item 14 „It is unnatural for my mind and body to be controlled by medications" (3.5±1.6 vs.2.9±1.9) and item 15 "My thoughts are clearer on medication" (3.6±1.6 vs 4.0±1.9). All these items belong to the negative and positive aspects of drug treatment subscales. In our sample the attitude towards drug treatment was definitely more negative than the

attitude assessed in the original sample. This difference can be observed as well when comparing the scores of the subscales: in our sample the scores of the Negative Aspects of medication and Psychological Reactance subscales were higher compared to the original Spanish sample. This can probably be explained by the difference between the two samples: in the original study ambulatory care patients were enrolled. We studied psychiatric patients requiring hospital treatment possibly with more severe symptomatology, thus, the appearing difference between these item scores can rather be considered as a proof of sensitivity and reliability of the questionnaire. Nevertheless, it is important to emphasize that drug treatment started during hospitalization is a determining experience for the patient. The early negative feelings towards medication may affect negatively the adherence at a later stage, when the patient will receive ambulatory care.

In our study the scores of the PHBQPT of the Hungarian sample were comparable to the scores published by the Spanish authors of the original scale.

4.2. Patient's control beliefs, motivations and current affective symptoms in association with the psychiatric treatment

In our research we used a new questionnaire, the PHBQPT in order to assess the patients' attitude towards treatment and health locus of control in correlation with the emotional state and the affective-motivational system. In order to identify specific patterns of the different attitudes, we created the dominant treatment attitude (DTA) for the scores of the five subscales which were higher than the average subscale score. The results have shown that all DTA-s were present in equal proportion in the sample, with the exception of Psychological Reactance which proved to be the rarest. Considering that some subgroups can be characterized by more than one DTA-s, we assessed the occurrence of multiple carriers and found that the double DTA carriers are the most frequent. Among the double DTA carriers the Doctor HLOC+Positive Aspect and the Doctor HLOC+ Internal HLOC carriers have been shown to be the most common. Regarding the distribution of the HADS and BIS/BAS scores, the sharpest difference could be observed between the carriers and non-carriers of the Doctor HLOC+Internal HLOC DTA. At the same time, the anxiety and depression subscale scores were much

lower (the depression subscale score was lower approximately by the half) in the case of the carriers of the Internal HLOC+ Doctor HLOC DTA. The analysis of correlation of DTA and BIS/BAS scale scores has shown that the PosAsp and Doctor HLOC correlates with Reward Responsiveness, while the Internal HLOC and the Psychological Reactance correlates with BAS Drive. We did not find correlation between the Negative Aspect and any other subscale. The Positive Aspect, Doctor HLOC and Internal HLOC subscales correlated with lower scores on the depression subscale of the HADS, however, the higher scores on the Psychological Reactance subscale were related to lower depression scores, but higher scores on the anxiety subscale. When comparing the different diagnostic categories, the most noticeable difference could be observed between the group of patients with affective disorders and psychotic disorders: the Doctor HLOC score was higher in the former group. The BAS Fun Seeking subscale score was lower in the group of patients with affective disorders than in the group of personality disorders.

The correlation between the attitude of patients towards treatment and their treatment adherence has been evaluated by several researchers. Lower self-efficacy, negative attitude towards drugs and poor insight correlate negatively with adherence [2, 54, 55]. Control preference correlates negatively with adherence [36] and the shared decision making and higher trust towards psychiatrists have correlated with stronger adherence [36, 56-58]. Non-adherence has been found to occur more frequently in the case of patients with higher scores on the external locus of control subscale [59]. The connection between the attitude towards drugs and treatment adherence has been assessed in several studies. Pharmacophobia leads to poor adherence [11, 36, 60] and the acceptance of treatment depends on the level of worrying about side-effects [11, 36, 60-62].

In spite of the large amount of studies regarding adherence and attitudes toward treatment, the psychobiological background of these factors has not yet been extensively studied. In our sample of psychiatric inpatients the higher score on Positive Attitude towards drug treatment scale was the most frequent finding and there were less patients with high Psychological Reactance. This finding is encouraging and is in contradiction with the general belief that in the case of psychiatric patients, especially in hospital settings, the negative attitude towards treatment is characteristic. It is concordant with

the findings of our earlier publication, in which we reported that drug attitude did not differ significantly between the psychiatric and non-psychiatric subgroups [51].

The majority of research data refers to the adherence of schizophrenic patients, which show that the rejection of drug treatment occurs frequently at the beginning of the treatment. Our results have shown that this rejection is not related to Psychological Reactance (this is not higher in the group of schizophrenic patients compared to patients treated for affective disorders) but to the lower score on the Doctor HLOC subscale. We found correlation between Psychol React and BAS Drive, between the Doctor HLOC and Reward Responsiveness and between PosAsp and Reward Responsiveness as well. The latter correlation points to the importance of the reward system sensitivity regarding the presence of Positive Attitudes. There is also an important correlation between the reward system sensitivity and the Positive Aspect and the Doctor HLOC as well. The role of the reward system was more pronounced in the case of patients with depressive symptoms; while in anxiety disorders a higher BIS sensitivity was present. Considering this, it can be concluded that rewarding techniques can help to strengthen PosAsp and Doctor HLOC in case of patients with more severe depressive symptoms but might probably be less efficient in case of anxiety. Surprisingly, there was no correlation between the Negative Aspect of drugs and the BIS/BAS or depressive symptoms. We can conclude, that while the locus of control is related to the biologically determined affective-motivational system and the current affective state, the Negative Aspect is independent of these. The latter is mostly related to experiences acquired in adulthood and not during earlier stages of life, it is not the result of factors influencing the developing nervous system, in other words, it can be modified using psychotherapeutic and/or educational techniques (Figure 6).

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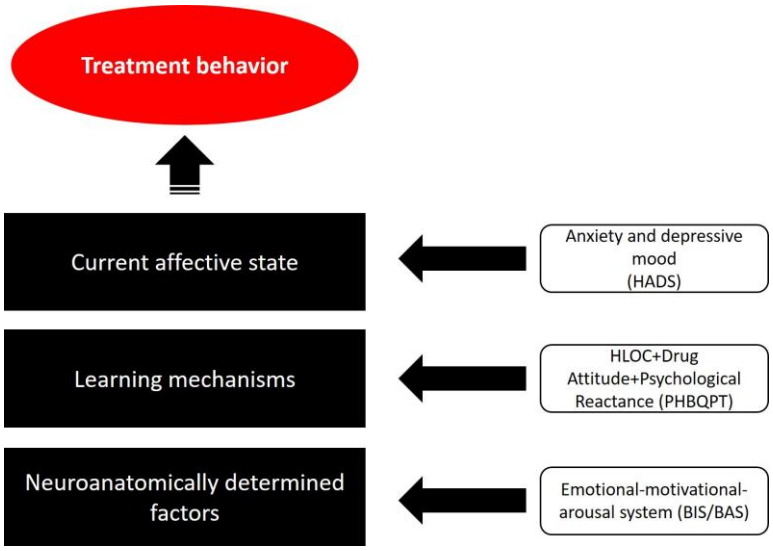

Figure 6 The different levels of influencing factors of the treatment behavior [50]

The physician has to identify the attitudes toward treatment which can be modified so that efficient adherence-improving interventions can be planned (Figure 7).

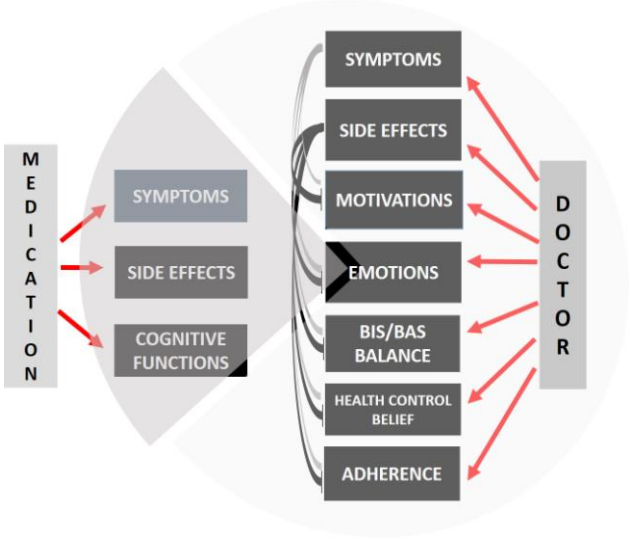

Figure 7 The effects of medication and the doctor's influence [32]

4.3. Health control belief and attitude toward treatment in psychiatric and non-psychiatric clinical samples

This is the first report on a comparative analysis of drug attitude and health concept of different clinical samples. Despite the fact that drug adherence is a hot topic in clinical psychopharmacology and it is generally considered that psychiatric patients are less adherent with their treatment and mistrust toward medication is more common among them compared to the non-psychiatric patient population, there have not been any direct comparisons regarding these aspects in psychiatric and non-psychiatric subsamples so far. The analysis of different samples may provide valuable information which could help us better understand the specific features and the general common mechanisms behind the attitudes toward treatment of patients suffering from different chronic diseases. This information can be used to develop more efficient interventions to improve adherence.

Poor treatment adherence leads to an enormous healthcare and economical burden. According to Krueger et al. (2005) [63], self-reported data overestimate medication adherence in clinical practice by as much as 200%. Lapane et al. [64] demonstrated that while doctors estimated that 9% of patients do not talk about their non-adherence, in reality 83% of patients reported that they would never tell their physician if they did not plan on picking up a prescription. According to some financial analyses, non-adherence leads to an annual loss of 100–300 billion dollars in the United States (IMS Institute for Healthcare Informatics). Certain estimations suggest that improving adherence to diabetes medication would prevent 699,000 emergency department visits and 341,000 hospitalizations each year in the United States of America [65]. Some statistical data suggest that 33–69% of the hospitalizations are related to poor adherence [7].

The results of our study have shown that there is a more robust difference regarding attitude toward medication between ADDICT patients and GEN PSYCH patients than between the latter population and NON-PSYCH subjects. Although positive aspects of medication appeared more pronounced in the GEN PSYCH sample, trust in doctors and feelings of personal responsibility for their own health were present

at a higher level among patients with addictions. Participants belonging to the GEN PSYCH sample were more skeptical regarding the importance of seeing their physician than patients treated due to somatic diseases, as it is shown by the reduced Doctor HLOC subscale score. GEN PSYCH patients do not believe that regularly seeing their doctor would decrease the risk of getting worse and they do not think that "following the doctor's order to the letter" is the best way to keep their condition from getting any worse. Analyzed together with other items of the scale, it can be concluded that GEN PSYCH patients believe that they might need some help, but they frequently refuse to follow the instructions of medical professionals. However, according to the Positive and Negative Aspect subscale scores, beliefs and attitude towards medication do not differ significantly in the GEN PSYCH and NON-PSYCH samples.

According to the results of recent studies on treatment adherence conducted by De las Cuevas, to which our group also contributed, some factors can have specific effects on adherence in the case of different dignostic groups. High psychological reactance was associated with decreased adherence in patients treated for depression[66], high internal locus of control scores were associated with poor adherence in patients with schizophrenia [67], while high doctor locus of control scores were significantly associated with increased adherence only in patients with bipolar disorder [68-70].

Despite the fact that in the NON-PSYCH sample there were higher levels of external locus of control than in the psychiatric group, it seems that the level of mistrust toward medication is similar in both samples. These results are in concordance with the conclusions of a review published by Brown et al. [71]. They emphasized that besides individual experiences, the increasing mistrust of societies toward healthcare systems contribute to the negative beliefs. The authors highlighted that patients' negative beliefs are often stronger than their clinicians would suppose. An important factor contributing to patients' mistrust is the assumed relationship between the pharmaceutical companies and doctors. Grande et al. reported that 55% of patients believed that their doctors received gifts from the companies and this belief was associated with lower trust in their physician and doubled the chance of mistrust in the entire healthcare system [72]. Another factor leading to mistrust was the contradiction between the information

acquired from different sources (healthcare provider, media, internet) [71]. De las Cuevas et al. (2014) found that highly psychologically reactant patients were more likely to be noncompliant; they generally resist any guidance or assistance [36].

Mago et al. (2018) reported that in a sample of 2,096 subjects suffering from major depressive disorder the most frequent negative emotion reported by patients regarding their medication was frustration (29.8% of respondents) [73]. Concerning feelings about their healthcare providers, the majority reported trust, confidence and feeling understood but almost 20% reported frustration due to not feeling heard, ineffective treatment, and feeling rushed. The reasons for frustration with medication were lack of efficacy and tolerability issues. In contrast, physicians estimated that only 11% of patients were frustrated with their medications and 5% with healthcare quality [73]. In another survey, data of 3,684 subjects were analyzed concerning adherence to antidepressant treatment. They found that 22% was the overall level of adherence, thus only one in four patients complied with treatment. Surprisingly, better adherence was observed in patients with polypharmacy [74].

For a successful therapy, one needs to understand patients' health beliefs and attitudes towards drug treatment. It is also essential that patients at their first encounter with mental health care professionals are given comprehensive and appropriate information regarding the planned treatment [75].

4.4. Analysis of the change of treatment attitude after pharmacological treatment

According to the results of our pilot study, the Negative Aspect of drug treatment score decreased and the Doctor HLOC and Internal HLOC scores increased significantly during the treatment. These favorable changes were regardless of the nature of the disorder for which the patients required psychiatric care. The results of regression analysis have shown that there is correlation between the extent of decrease of Negative Aspect subscale scores and the decrease of anxiety and depressive symptom scores. Besides this, there is also correlation between the extent of decrease of depressive symptom scores and the increase of scores of Positive Aspect of drugs subscale. It is important to mention, that although the neurocognitive functioning of the

patients improved during their treatment, this improvement did not have a significant influence on their attitude toward drug treatment, health locus of control and psychological reactance. The results of our previous research have shown that no significant difference could be found between the attitude toward drug treatment of patients treated for somatic illnesses and those who required treatment for psychiatric disorders [51]. Our results have some implications on a current problem, the COVID-19 vaccine rejection. The effective treatment of anxiety and depressive symptoms may influence favourably the attitude toward treatment of the patients, regardless of the diagnosis or the nature of therapy, and it may facilitate the acceptance of COVID-19 vaccination as well.

The results of a large number of studies have shown that the incidence of anxiety and depressive symptoms increased significantly in the general population since the onset of the COVID-19 pandemic. According to the results of a survey involving more than 71000 people, 31% of this population presented anxiety symptoms while the occurrence of depressive symptoms was 28%. In the case of subjects with confirmed COVID-19 and their family members the risk of depression and anxiety was higher than the risk of the non-affected persons (depression: adjusted odds ratios: 3.27 for patients; 1.53 for family members, anxiety: adjusted odds ratios: 2.48 for patients; 1.53 for family members) [76]. According to the results of an international survey, 25% of the participants presented anxiety symptoms and 23% of the respondents could be diagnosed with depression [77]. The results of a Libyan online survey have shown that depressive symptoms could be identified in the 46% of respondents, while the anxiety symptoms were present in 19% of them in the summer of 2020 [78]. According to the results of a Canadian study, the occurrence of affective disorders among young adults did not change during the first wave of the pandemic compared to the previous period, but the incidence of severe cases increased significantly [79]. An increasing occurrence of severe affective symtoms can be expected in the upcoming period as a result of the social and economical impacts of the pandemic. Considering our results regarding the negative impact of depressive symptoms and anxiety on the Negative Aspect of medication subscale score, the assessment and treatment of affective symptoms may have a positive influence on COVID-19 vaccine acceptance.

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5. Conclusions

We can conclude that PHBQPT can be used for the evaluation of a very complex psychological construct composed by elements which are part of a multivariable model of the treatment behavior of patients with psychiatric disorders. The use of the scale in clinical practice may be useful for the detailed evaluation of the attitude of patients toward treatment which may help in planning the adherence-improving interventions necessary during long-term therapy. The evaluation of dominant treatment attitudes can be a useful method for studying the different types of combination of health control beliefs, drug attitude and psychological reactance in patients with psychiatric disorders. The behavioral activation and inhibition system and the current affective state influence the dominant treatment attitudes in a specific manner, depending on the types of combination of DTAs. Our findings suggest that mistrust toward medication did not differ between the GEN PSYCH and NON-PSYCH samples, while acceptance of the doctor's competency was stronger in the non-psychiatric subsample. According to our results, there is a stronger correlation between the emotional state of patients and their attitude toward treatment than between the latter and the level of their neurocognitive functioning. The improvement of affective symptoms was associated with decreased Negative Aspect and increased Positive Aspect subscores, a change which was independent of the diagnosis of patients. Based on our results, the modification of the relevant cognitive and emotional-motivational factors can be planned at the start of the therapy in order to establish a better treatment adherence. More attention needs to be paid to the changeable background variables of control beliefs and attitudes toward treatment in order to implement efficient adherence-improving interventions by the physician.

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6. Summary

In our studies we have analysed the health control beliefs, drug attitude and psychological reactance with the help of a recently developed complex questionnaire. We have performed the Hungarian validation of this instrument in a sample of Hungarian psychiatric patients and confirmed its reliability and consistency. With further investigation certain associations have been revealed on the effects of affective and motivational state and treatment behavior. Moreover, we have introduced the concept of the dominant treatment attitude. We have found that Doctor HLOC was the most common dominant attitude and approximately 70% of the sample had more than one dominant treatment attitude. The Behavioral Activation and Inhibiton System and affective symptoms had specific effects on the treatment attitude. In the following stage we compared the treatment attitude of patients with and without psychiatric disorders. Our findings suggested that there was no significant difference between the drug attitude of the two groups, however, the Doctor HLOC scores of patients with psychiatric disorders were lower than of patients with somatic disorders. Finally, a significant change of the PHBQPT scores could be observed after a 14-day treatment, which was the result of the improvement of affective symptoms, regardless of diagnosis. The results of our studies highlight the importance of assessment of health control beliefs and attitude towards drug treatment both in clinical practice and scientific research, making possible the identification of modifiable factors of treatment behavior and attitude towards treatment in the psychiatric patient population.

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8. Bibliography of the candidate's publications I. (related to the thesis)

Articles

Pogany, L. and Lazary, J.(2019) Pharmacological treatment and health control beliefs from the perspective of psychiatric patients: differences in attitudes Neuropsychopharmacol Hung 21 (4): 170-178.

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Poster

Pogány László, Lazáry J.: Health locus of control and drug attitude: differences between psychiatric and non-psychiatric samples (33rd Congress of the European College of Neuropsychopharmacology, 12-15 September 2020, virtual congress)

9. Bibliography of the candidate's publications II. (not related to the thesis)

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bipolar disorder: the psychiatrist may have more influence than in other severe mental illnesses Neuropsychopharmacol. Hung 23(4): 347–362

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