DRUG ATTITUDE AND HEALTH CONTROL BELIEFS OF PSYCHIATRIC PATIENTS

PhD thesis

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Introduction

Attitude towards drug treatment has an important influence on therapeutic outcome. This topic is of special relevance to the overcoming of the COVID-19 crisis, which is hindered by vaccine refusal despite of the proven infection of 220 million people and the death of five million worldwide. This 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. The assessment results of the potential influencing factors of the complex behaviour of medication taking have shown that clinical and sociodemographic factors were less powerful predictors of adherence than the beliefs regarding medication treatment. The theory of locus of control was adapted by Wallston to health related fields of research. Wallston proposed a multidimensional scale in his research on health behavior (Multidimensional Health Locus of Control Scale, MHLC scale). Generally, the MHLC scale is used together with other questionnaires, and provides additional information for the complex evaluation of the results. Although it was once thought that internal and external beliefs were at opposite ends of a continuum, 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).

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. 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), to one's own actions (Internal HLOC) and psychological reactance (Psychol React). The 17-item PHBQPT was compiled from the Drug Attitude Inventory (DAI-10), the MHLC Form C [1] and HPRS scales. 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 the identification of intervention objectives.

1. Objectives

The following research objectives have been determined:

I. Validating analysis of the Hungarian version of 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, multiple carriers and 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 attitude towards treatment as a result of relevant therapy and analysis of associations between change of treatment attitude and change of affective symptoms and change of cognitive improvement.

2. Methods

The enrolled patients were recruited from the departments of the National Institute of Mental Health, Neurology and Neurosurgery , Budapest, Hungary (former name: Nyírő Gyula National Institute of Psychiatry and Addictions). Five patient groups were created based on the ICD-10 codes (addictions-F1x; psychotic disorders-F2x; affective disorders-F3x; anxiety disorders- F4x; and personality disorders-F6x). All subjects agreed to participate voluntarily in the study after an informed consent process. We did not enroll patients living with mental

retardation, having neurocognitive disorder or patients who were hospitalized involuntarily. The study was approved by the Hungarian Central Ethical Committee, Budapest, Hungary (number of approval: 45735-5/2020). For the statistical analyses we used SPSS 24.0 software.

3.1. Validation of the PHBQPT

A dataset of 188 patients (115 women and 73 men; mean age 32,8±10,7 years) treated at the departments of general psychiatry was analyzed in this study. We used the Hungarian version of the Patient's Health Belief Questionnaire on Psychiatric Treatment (PHBQPT) which was translated by our group. The translation was back-translated by an independent person to English, the comparison of this text with the original was done by a native speaker.

The normality of distribution has been tested by the Kolmogorov-Smirnov test. Internal consistency and correlations of items have been evaluated by reliability statistics. We calculated scale mean if subscale was deleted for structural analysis. Factoral analysis has been performed by use of principle component analysis (PCA) with Kaiser rotation method.

3.2. Association analysis of the affective and emotional effects and PHBQPT

A dataset of 295 inpatients (Mean age: 45.9±14.8; 162 women and 133 men) treated for psychiatric disorders was analyzed in this study. The Hungarian version of PHBQPT, Behavioral Inhibition/Activation System Scale (BIS/BAS) and Hospital Anxiety and Depression Scale (HADS) were used for measurements. We created a 'dominant treatment attitude' (DTA) variable from the 5 subscales of PHBQPT based on the mean value of the scores.

Chi-square tests were performed in case of binary variables. The effects of age and gender on the dependent variables were calculated by general linear model.

3.3. Analysis of the PHBQPT scores in psychiatric and non-psychiatric samples

A total of 189 participants were recruited from departments of general psychiatry (GEN PSYCH, n=112), a department of addictology (ADDICT, n=42), a department of internal medicine (IM, n=20) and a department of neurology (NEUR, n=21). The patients treated at the department of addictology were admitted to the department after a motivational interview. Patients from IM and NEUR were selected to participate in the study if they were treated with at least one psychotropic medication (generally an anxiolytic). For comparative analysis 3

subgroups were created: the general psychiatry (GEN PSYCH); addictology (ADDICT); and IM and NEUR (NON-PSYCH).

To assess the differences between clinical subgroups (GEN PSYCH vs. ADDICT and GEN PSYCH vs. NON-PSYCH),we used one-way ANOVA with Tukey's post hoc test or t-test in case of normal distribution.

3.4.   Change of health control beliefs after a 2-week treatment

A dataset of 84 psychiatric inpatients (45 women and 40 men; mean age: 42.9±13.5 years) was analyzed in this study. The enrolled patients received pharmacological treatment, supportive therapy and participated in different group therapies. Anxiety and depressive symptoms were evaluated with the aid of the two subscales of HADS (HADS-Anx and HADS-Dep). Neurocognitive performance was assessed with the Trail Making Test (TMT-A and TMT-B) and Stroop test. The patients filled the PHBQPT and HADS questionnaires on the day of their admission to the department, the neurocognitive tests were performed on the same day as well. All assessments were repeated after two weeks of treatment.

The score changes of the scales were tested with paired t-test, the correlation of the score changes were tested with generalized linear model.

4.   Results

4.1. The validation and analysis of PHBQPT in a sample of Hungarian psychiatric patients

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 internal consistency of the whole scale is acceptable (Cronbach's alpha=0.62). The use of 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 the 5-factor model it was 60.8%. Thus, the factorial analyis confirmed the validity of the 5-subscale structure in our sample. The correlation matrix of the subscales resulted in values similar to the original description of the scale. Effects of gender were not significant on either subscales ($p>0.05$ in all cases).

The distributions of the subscale scores 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 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 Cronbach's alpha of the Doctor HLOC is 0.65. The mean of single items is 5.04 and the variance is 1.24. 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. The internal consistency of the PsycholReact subscale is weak (Cronbach's alpha=0.25). The means of single item is 3.81 and the variance is 2.04.

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

### 4.2.1. Analysis of the structure and prevalence 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. 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.

4.2.2. Quantitative and qualitative analysis of multiple DTA prevalence

With regard to the fact that PHBQPT subscales are meant to describe the complexity of factors influencing drug adherence, in spite of their 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. In order to analyze the variations of the concomitantly occurring DTA-s, we assessed the frequency of occurrence of different DTA carriers. 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
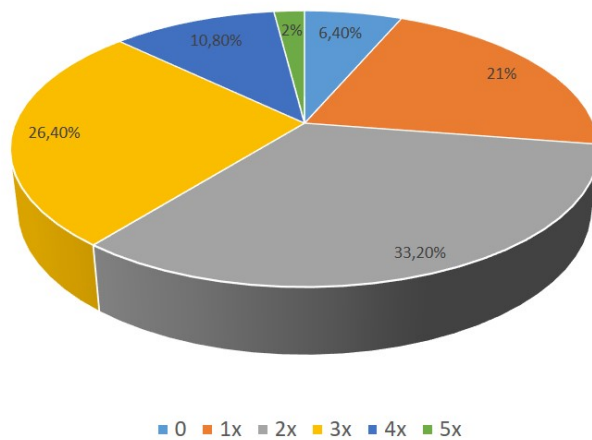
0=no DTA; 1x= one DTA; 2x=2 DTA; 3x=3 DTA; 4x=4 DTA; 5x=5 DTA

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 PosAsp-Internal HLOC and HADS-DEP score. The carriers of this DTA reached a lower score on the HADS-Dep than the non-carriers (p=0.07). The Doctor HLOC-Internal HLOC pair separated most sharply the sample regarding the anxiety and depression subscale scores. 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.

4.2.3. 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 is differentiated from the other factors through the higher score of Reward Responsiveness, while the 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 DTAs were of protective value against

depressive symptoms (Table 6). Interestingly, the 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 except for 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.

4.2.4. Differences of PHBQPT, BIS/BAS and HADS scale scores among the diagnostic categories

We analyzed the difference between diagnostic categories regarding the scores of the phenotype questionnaire. Our results did not show major differences between the groups, apart from 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 in the case of patients treated for affective disorders (p=0.008; Table 7).

Table 7 Differences of the PHBQPT, BIS/BAS and HADS scale scores in different diagnostic categories

	F2	F3+F4	F6	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 the Tukey's post hoc tests are presented.

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

4.3.1. 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 to the results of the study of De las Cuevas et al (2019) [4]. 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 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; $p=0.01$). With regard to PHBQPT subscales, NON-PSYCH participants scored significantly higher on the 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.

4.3.2. Comparison of the 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 the Doctor HLOC, Internal HLOC and Psychological Reactance subscales (all p-values<0.05). Patients with addictions scored higher on the Doctor HLOC subscale than patients with psychotic (F2x) and affective (F3x) disorders. Further, patients with addictive disorders also scored higher on the Internal HLOC subscale compared to the subjects with psychotic (F2x), affective (F3x) and anxiety (F4) disorders (Figure 4).

Figure 4 Significant differences of Doctor HLOC and Internal HLOC subscale scores among the diagnostic categories.
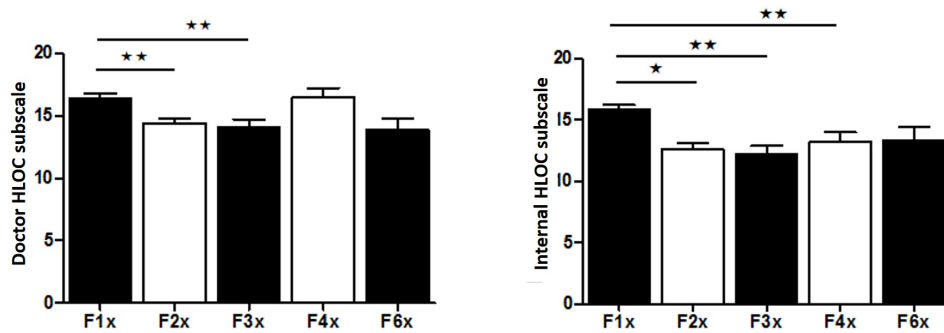
4.3.3. Comparison of the three clinical subgroups

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 (pANOVA= 0.004); Doctor HLOC score was lower in the GEN PSYCH compared to the ADDICT and to the NON-PSYCH (pANOVA= 0.002 and 0.04, respectively); Internal HLOC score was higher compared to the GEN PSYCH (pANOVA= 8×10^{-7}), and Psychological Reactance score was higher in the ADDICT compared to the GEN PSYCH (pANOVA= 0.04) (Figure 5).

Figure 5 Significant differences of PHBQPT subscale scores among the psychiatric, non-psychiatric and addiction subgroups.
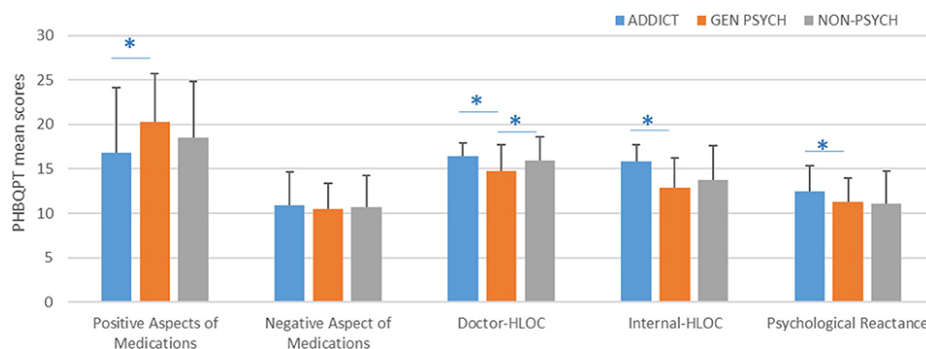
4.4. Analysis of the change of treatment attitude after pharmacological treatment

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.

Table 10 Associations of the delta values of PHBQPT subscale scores, HADS scores and neurocognitive tests.

	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. Conclusions

We conclude that PHBQPT can be used for the evaluation of a very complex psychological construct composed of 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 towards 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 health control belief combinations, drug attitudes 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 DTA combinations. 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 towards 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 variables in the background of control beliefs and attitudes towards treatment to implement efficient adherence-improving interventions by the physician.

5. 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 behaviour. 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 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 adherence in the psychiatric patient population.

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

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