

# Somatic and cognitive markers in bipolar affective disorder and schizophrenia

PhD Thesis

Timea Csulak, MD

Supervisor

Prof. Tamás Tényi, MD

Róbert Herold, MD

Doctoral School of Clinical Neurosciences (D221)

Leader of Doctoral School: Prof. Sámuel Komoly, MD

B- 1/2012 Program of Psychiatry

Head of Program: Prof. Tamás Tényi, MD



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## **I. Introduction**

Psychiatric disorders are characterised by a wide range of symptoms; patients with the same diagnosis show considerable heterogeneity in their symptoms. The search for reliable biomarkers has long been a focus of psychiatric research. This involves the search for clinically useful biological features that are associated with pathophysiological variations of etiological significance in the disease. A valid biomarker may lead to a more accurate diagnosis and therapy, but may also help to understand the nature of the pathophysiology underlying psychopathology (Iacono, 1985). Endophenotypes are quantitative biomarkers (such as neurocognitive and neurophysiological abnormalities, brain imaging lesions, metabolic values, etc.). Endophenotypes identify psychopathology risk prior to its onset and can be used to identify etiologically relevant genetic variants (Iacono et al., 2017).

In psychiatric genetics, the criteria proposed for the identification of markers have been adapted to endophenotypes (Gottesman and Gould, 2003), which are used to define the endophenotype:

1. linked to a specific disease in the population
2. the endophenotype is inherited
3. condition independent, detectable at any stage of the disease
4. shows familial cumulation
5. the patient's endophenotype is more prevalent in asymptomatic relatives than in the general population

The origin of both schizophrenia and bipolar affective disorder is multifactorial.

The neurodevelopmental deficits underlying their development have been demonstrated in several studies (e.g. Yücel et al., 2002; Vogeley et al., 2000).

Classically, bipolar affective disorder has been treated as a separate entity from schizophrenia, often referring to the Kraepelin dichotomy. In contrast, several studies have demonstrated a genetic link between the two disorders (Lichtenstein et al., 2009; Owen et al, 2007), and similar neurometabolite and protein abnormalities in these

diseases (Kraguljac et al., 2012; Goldsmith et al., 2016); similar brain morphological changes have also been described (Arnone et al., 2009). Based on these results, suggesting that a number of common biological factors are responsible for the development of clinical symptoms in both diseases, which also overlap, it is likely that bipolar affective disorder and schizophrenia are located on the psychosis continuum. The biomarkers identified in the psychosis continuum can be important in making a more accurate diagnosis and in selecting a more appropriate therapy. They may also help to understand better the underlying processes of the disease. The research of our group so far has largely focused on two biomarkers, minor physical anomalies (MPA) and mentalizing (Herold et al., 2002; Tényi et al., 2009; Hajnal et al., 2014; Tényi et al., 2015; Berecz et al., 2017; Varga et al., 2021). In our study, we continued previous studies of MPAs and mentalizing in the psychosis continuum disorders, bipolar affective disorder and schizophrenia.

## **II. Minor physical anomalies in first-degree relatives of patients with bipolar I affective disorder**

### **Introduction**

MPAs are clinically nonsignificant errors of morphogenesis which have a prenatal origin and may bear important informational value; they are sensitive indicators of altered embryonic development and may be somatic markers of neurodevelopmental dysfunction, as both the nervous system and the skin are derived from the ectoderm. They develop in the first and/or early second trimester of pregnancy (Méhés, 1988; Tényi et al., 2004) and are potentially valuable indicators of early aberrant neurodevelopment. Once they develop, they persist into adulthood and can be detected by visual examination of the body part (Hajnal et al., 2016).

The endophenotypic concept of bipolar affective disorder is an important approach to elucidating the pathogenesis of the disorder. Some studies have found no significant

difference in the prevalence of MPAs between patients and subjects (Alexander et al., 1994; Green et al., 1994). In contrast, several studies have described a higher prevalence of MPAs in patients (Berezcz et al., 2017; Varga et al., 2021).

Only one study has examined the prevalence of MPAs among healthy, asymptomatic first-degree relatives of patients with bipolar affective disorder, with a very low number of cases, finding no significant differences between relatives of patients and healthy controls (Green et al., 1994); therefore, we consider the study of MPAs among asymptomatic first-degree relatives of patients with bipolar disorder to be an open area for further research.

## **Objectives**

The aim of this study was to investigate the prevalence of minor physical anomalies - using the Méhes Scale to differentiate minor malformations and phenogenetic variants - in the relatives of patients with bipolar I disorder comparing them to normal control subjects. The following hypotheses have been tested: (1) MPAs are more prevalent in the relatives of bipolar I patients compared to normal controls, which supports the hypothesis, that MPAs can be endophenotypic markers of bipolar I disorder (2) a higher rate of MPAs is found predominantly in the craniofacial regions among the relatives of bipolar I patients, pointing at aberrant early (first and second trimester) neurodevelopment.

## **Methods**

20 first-degree healthy relatives of patients with the diagnosis of bipolar I disorder were examined. Eleven parents, 3 siblings and 6 children were included in the study. As a comparison 20 normal control subjects matched for sex, age and ethnic origin were also observed for minor physical anomalies.

We have used the Méhes Scale for evaluation of MPAs, which includes 57 minor signs. MPAs were connected to body regions for comparison. A clear differentiation between minor malformations and phenogenetic variants were introduced, the scale and detailed definitions were published earlier (Trixler et al., 2001). The Committee on Medical Ethics of University of Pécs accepted the proposal for the study (No.6416).

Before the statistical analyses interrater reliability was tested and the kappa coefficient was  $>0.75$  for all items. Statistical analyses were done by applying the Mann - Whitney U-test for and the chi-squared test for the comparison of the two groups with each other. Two-sided Fisher's exact tests were used to compare the two groups with each other by body regions. The level of significance chosen was  $p < 0.05$ . All the statistical analyses were done by the use of SPSS Version 21.

## **Results**

The comparison of two groups with the Mann-Whitney-Utest showed significant differences between them (relatives of bipolar I patients: mean rank: 29.8 vs. normal controls: mean rank: 11.2,  $p < 0.001$ ).

We did a dichotomization by establishing two groups: (1) none or only 1 MPA, (2) MPAs more than 1. While in the control group the number of individuals with none or only with 1 MPA was 18 (90%), this in the relative group was 2 (10%), the chi-squared test showed a statistically significant difference ( $p < 0.001$ ). The first group of relatives of patients with bipolar affective disorder included 2 people. We found more than 1 MPA in 18 relatives' cases.

Relatives of bipolar I patients showed a higher frequency of MPAs in the ear, head, mouth and trunk regions compared to normal control subjects.

By the differentiation of minor malformations and phenogenetic variants, we have found that phenogenetic variants were more common among the relatives of bipolar I patients compared to the control group (relatives: mean rank: 26.15 vs. controls: mean rank: 14.85,  $P = 0.002$ ), while minor malformations were also more prevalent in the

relative group, (relatives: mean rank: 28.43, controls: mean rank: 12.57,  $p < 0.001$ ). Comparing phenogenetic variants by body regions, between the two groups phenogenetic variants in the mouth region were more prevalent (Fisher's exact test, two-sided: 0.003) among the relatives of bipolar I patients. Comparing minor malformations by body regions: ear minor malformations (Fisher's exact test, two-sided: 0.008), trunk minor malformations (Fisher's exact test, two-sided: 0.025) and foot minor malformations (Fisher's exact test, two-sided: 0.047) were more prevalent in the relative group.

In the individual analysis of minor anomalies one minor malformation (sole crease) and one phenogenetic variant (high arched palate) were more prevalent ( $p = 0.047$ ) in the bipolar relatives group compared to the normal control group.

## **Conclusion**

This is the first report in literature on the increased prevalence of minor physical anomalies among the first-degree unaffected relatives of bipolar I patients. Our results on the overrepresentation of the examined anomalies in the relatives of bipolar I patients support the hypothesis, that MPAs may be endophenotypic markers of bipolar I affective disorder. In considering the concept of endophenotype, it should be remembered that although MPAs are not specific for bipolar affective disorder, this is the first, ground-breaking finding of these markers in relatives of patients with bipolar I affective disorder.

Based on our results, we highlight that insults resulting in abnormal neurodevelopment can occur both during the first and second trimester and thereafter (as both phenotypic variants and minor malformations were more prevalent in the matched individuals).

Importantly, we found that relatives of bipolar I patients had a higher frequency of MPAs in the eye, head and mouth, and one phenogenetic variant (gothic palate) was more frequent in this group. Previous findings suggest that anomalies in the head and

mouth may be more relevant to the neurodevelopmental disorder hypothesis (Méhés, 1988; Ince et al., 2020; Tényi et al., 2015).

### **III. Implicit Mentalizing in Patients With Schizophrenia: A Systematic Review and Meta-Analysis**

#### **Introduction**

Mentalizing (or mentalization, theory of mind) is a key aspect of social cognition. During the processes of mentalizing we attribute mental states (intentions, beliefs, desires, emotional states) to ourselves and others, which enables us to understand and predict social behavior. Several researchers assume that mentalization is based on two systems, an explicit and an implicit one (Apperly and Butterfill, 2009; Butterfill and Apperly, 2013). Implicit mentalizing is supposed to be present very early, presumably from birth. It is characterized by fast and pre-reflexive non-verbal information processing, which is decoded without awareness. In contrast to this intuitive ability, the explicit form of mentalizing is inferential, relatively slow, and it relies heavily on verbal and conscious information processing. It develops parallelly with linguistic and cognitive skills (e.g., executive functions). The implicit-explicit systems are likely to persist and coexist throughout the lifespan (Apperly and Butterfill, 2009; Butterfill and Apperly, 2013; Vogeley, 2017). A recent meta-analysis of imaging data found significant overlap between the two types of processing, although important differences in the location of activation were also observed (Molenberghs et al., 2016).

In schizophrenia, it is now evident that social cognition is significantly affected and there is, among other things, a significant mentalizing deficit. Mentalizing impairments are characteristic both in the acute and the remission phases, and they can be detected in first-degree, clinically asymptomatic relatives (Herold et al., 2002; Herold et al., 2018). Mentalizing may be deficient even before the onset of the disease, may predict

psychotic conversion, and often worsens before the first episode (Bora and Pantelis, 2013; Davidson et al., 2018; Tikka et al., 2020).

Imaging studies have also revealed significant abnormalities in schizophrenia. In addition to the brain volumetric abnormalities in pre-frontal and temporal areas (Benedetti et al., 2009; Herold et al., 2009; Koelkebeck et al., 2013) associated with deficient mentalization, studies using different functional imaging procedures have undoubtedly described atypical neural activation characterized by over- and underactivation in mentalizing regions (Koelkebeck et al., 2013).

Despite the extensive research on mentalizing in schizophrenia, the majority of studies has been focused only on explicit mentalizing. Relatively little is known about potential alterations of implicit mentalizing. Based on the neurodevelopmental hypothesis of schizophrenia (Weinberger, 1987) we cannot exclude that the implicit mentalizing is also impaired, as early neurodevelopmental abnormalities may affect the neural networks responsible for implicit mentalizing, which in turn may influence the development of later explicit mentalizing skills.

Unaffected implicit mentalizing skills may represent a significant base for remediating the impaired explicit mentalizing skills. However, impaired implicit mentalizing can be a significant limit in remediation.

## **Objectives**

The aim of this systematic review and meta-analysis is to examine the nature of possible implicit mentalizing alterations in schizophrenia compared to healthy controls.

For theoretical clarity in our meta-analysis and systematic review we included only those studies that used non-verbal tasks to indirectly measure the accuracy with automatic behavioral signs without verbal answers. We excluded those studies that measure mentalizing skills with verbal answers or with spontaneous use of mental-state language.



This systematic review and meta-analysis were reported based on PRISMA Statement (Page et al., 2021). The review protocol was registered on PROSPERO (CRD42021231312). There was no protocol deviation.

## **Methods**

A systematic search was performed in four major databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science. The search date was 02.11.2020. The following search key was used: [(implicit) OR (spontaneous)] AND [(theory of mind) OR (mentalizing) OR (mentalization)] AND (schizophrenia). We searched in all fields/all text in every database. There were no restrictions or filters.

The search results were combined in a reference manager software (EndNoteX9; Clarivate Analytics, Philadelphia, Pennsylvania). Records were screened (after automatic and manual removal of duplicates) based on title, abstract, full-text. Then the references and citations of the full text screening records were reviewed. The selection process was conducted by two independent researchers (AH, TC). Disagreements were resolved by an independent third investigator (RH). Reference lists, publication citing (Google Scholar search engine) of the included studies were screened to find additional studies.

We included case-control studies which reporting on implicit mentalization function in patients with schizophrenia or schizoaffective disorder.

Studies which had overlapping populations were included only in the systematic review.

Two independent review authors extracted the following data from each eligible studies: first author, publication year, study design, country, number of centers, studied population, gender distribution, age distribution, number of patients; accuracy (in percentage), reaction time (in ms), mentalizing cue looking percentage, fixation duration, face looking percentage.

The “Quality In Prognosis Studies” (QUIPS) tool (Hayden et al., 2013) was used based on the recommendations of The Cochrane Prognosis Methods Group (PMG) by two researchers.

For continuous variables standardized mean difference (SMD) with 95% Confidence Intervals were calculated and since we had one study with sample size  $< 0.05$  was considered statistically significant difference. Random effects model was used to calculate the overall estimates using the DerSimonian-Laird (DerSimonian and Laird, 1986) method. Heterogeneity was tested using Cochrane’s Q and the I<sup>2</sup> statistics. As suggested by the Cochrane Handbook (Higgins and Green, 2011), I<sup>2</sup>-values were interpreted with the following levels: 0–40, 30–60, 50–90, and 75–100%, meaning “Might not be important,” “Moderate,” “Substantial,” and “Considerable,” respectively. Heterogeneity, with a  $p < 0.1$  considered significant. (Egger’s tests and funnel plots have not been carried out to assess any publication bias, because there was only a low amount of the studies included). All analyses were performed by R environment (R Core Team, 2021). To assess the certainty of the evidence we used the GRADE approach (Higgins and Green, 2011), which has four domains (risk of bias; inconsistency; indirectness; imprecision). The GRADE approach has four levels of evidence: high, moderate, low and very low. If there was a serious concern for any of the domains, we downgraded the evidence level.

## **Results**

The systematic search yielded 541 records. After checking the records and citation searching 11 publications remained. The 5 studies included in the quantitative synthesis examined 126 patients, while the 9 records included in the systematic review examined 157 patients.

## **Results of the quantitative synthesis**

For accuracy, we processed the percentage adequacy values of the response to the unrelated questions asked under the paradigms.

For this outcome, data from 5 studies (which used different paradigms) were used, involving 123 patients and 121 controls. There is a significant difference [SMD = -0.40; 95% CI (-0.70, -0.10);  $p = 0.008$ ] between patients with schizophrenia and controls with negligible statistical heterogeneity ( $I^2 = 22.0\%$ ) in performance during implicit mentalizing tasks. On average, schizophrenic patients have a weaker performance with an effect size of -0.40, which is considered medium effect.

As the performance of the two groups was identical in one study (Kronbichler et al., 2019) and we considered that the question asked was significantly simpler than in the other studies, we conducted a leave one out sensitivity analysis during which the heterogeneity decreased, the studies become completely homogeneous ( $I^2 = 0.0\%$ ) and the result remained significant and the effect size increased [SMD: -0.50; 95% CI (-0.78, -0.21);  $p = 0.001$ ].

For reaction time, data from 4 studies (using different paradigms) were used, including 77 patients and 81 controls. There is a significant difference in reaction time between the two groups [SMD: 0.89; 95% CI (0.36, 1.42);  $p = 0.001$ ]. On average, the reaction time was significantly longer in the schizophrenic group compared to the control group with a large effect size (effect size: 0.89). There is a moderate heterogeneity ( $I^2 = 57.00\%$ ).

## **Systematic review**

In a comparison of brain activation and deactivation patterns during mentalization tasks, patients with schizophrenia were found to have reduced activation in the right temporoparietal junction; bilaterally in the inferior frontal gyrus, similarly in the left

temporoparietal junction; left orbitofrontal cortex, right superior temporal sulcus and both left and right anterior cingulate cortex (ACC) compared to control individuals.

Functional connectivity analyses have also been performed, showing deficits in functional connectivity between the anterior cingulate and fusiform/parahippocampal gyrus in patients with schizophrenia. In controls, deactivation of the ACC was associated with an increase in activation of the right fusiform and parahippocampal gyrus, while in schizophrenia patients the opposite relationship was described with the fusiform and parahippocampal gyrus. Control individuals showed an increased BOLD response in the bilateral middle occipital gyrus in the spontaneous perspective taking situation.

All but one of the eye movement measurements (Roux et al., 2016b) described different eye movements in patients with schizophrenia compared to control subjects. One study described a longer looking time to contextual cues in patients, highlighting the importance of time in suggesting that patients' mentalizing is slower.

Two studies found longer average fixation duration in patients. In addition, Roux et al (2016b) demonstrated that fixation duration increases similarly with task complexity in patients and controls, indicating an equal increase in cognitive processing in both groups.

Three studies found shorter looking time for mentalization cues in patients with schizophrenia. One study found the same long looking times during Frith-Happé animation for patients and controls (Roux et al., 2016b). One study (using a chasing perception paradigm) described a central gaze strategy for patients during the perception of intentional motion (Roux et al., 2015). Patel et al. showed that patients' eye position was more variable than controls; the average area of the eye position was larger in patients. Patients spent less time viewing action regions of interest during intentional attribution tasks based on comic strips.

Three studies described patients spent less time looking at facial expressions. One of them described this discrepancy in peripheral field of view.

## **Conclusion**

Our meta-analysis and systematic review show that patients with schizophrenia have subtle impairments in implicit mentalizing.

The patients with schizophrenia exhibited a small but significant impairment in accuracy with negligible statistical heterogeneity and a medium effect size.

In contrast to accuracy, reaction time may reflect implicit mentalizing more closely (Kovács et al., 2010; Edwards and Low, 2017). Our meta-analysis revealed a significantly slower reaction time among patients with schizophrenia with a large effect size. It also suggests that implicit mentalizing is affected in patients with schizophrenia. Under the GRADE approach, the certainty of evidence was found to be low for accuracy and very low for reaction time.

Concerning functional imaging, differences in activation patterns during implicit mentalization tasks were found. The results suggest that patients with schizophrenia are likely to perceive communicative intentions, but may activate a different and probably less integrated neural network during implicit mentalization than control subjects.

The qualitative synthesis revealed some further characteristics of implicit mentalizing in schizophrenia. Patients with schizophrenia showed subtle deficits in visual processing, which is not surprising since studies of implicit mentalizing have predominantly used visual paradigms. It seems a relatively consistent result that visual scanning is inadequate and slower in patients than in controls. Patients tend to focus more on contextual cues instead of processing socially relevant cues. In addition, patients fixate less on the head region.

In conclusion, our results do not allow a firm conclusion at this moment. The substantial heterogeneity of the paradigms used in a small number of studies limit the generalizability of the results. Overall, in addition to the deficit of explicit mentalizing, implicit mentalizing performance is also affected in schizophrenia, if not to the same extent.

However, it would be important to have a clearer picture of the nature of implicit mentalizing in schizophrenia because it may significantly affect the remediation of mentalizing skills (Langdon et al., 2017), which in turn highlights the necessity of further studies.

#### **IV. Discussion**

The identification of appropriate biomarkers in psychiatric disorders is becoming increasingly important in psychiatric research, as they can significantly help to predict potential diseases, make diagnoses more accurate, identify subtypes within diseases and select more appropriate therapy. Somatic and social cognitive markers have been described for two of the disorders we have studied, bipolar affective disorder and schizophrenia. In our studies, we investigated the role of two biomarkers, MPAs and implicit mentalization.

In our first study, we detected MPAs in asymptomatic relatives of patients with bipolar I affective disorder, an indirect marker of neurodevelopmental disorders. The endophenotypic nature of MPAs has been confirmed by several studies. Some studies highlight the association of the head and mouth region with neurodevelopmental background (Trixler et al., 2001; Tényi et al., 2015; Berez et al., 2017), however, there is no complete agreement on this. Although, there have been fewer studies in bipolar disorder compared to schizophrenia, significant differences in the prevalence of MPAs have been found in patients with bipolar affective disorder compared to controls (e.g. Berez et al., 2017; Ince et al., 2020), a finding that was confirmed by our recent meta-analysis (Varga et al., 2021).

Only one study with first-order relatives has been conducted so far (Green et al., 1994), where no difference was found using the Waldrop scale with very low sample size. In our study, with a higher number of cases and with the use of the Méhes scale measuring much more variant, revealed a higher prevalence of MPAs among

asymptomatic relatives, confirming the endophenotypic nature of MPAs and emphasizing the neurodevelopmental background of bipolar affective disorder.

In our second study, we analysed the results on implicit mentalizing in a meta-analysis and systematic review. The relevance of this issue is underlined by the fact that impaired mentalizing functions can contribute significantly to psychosocial difficulties in patients with several psychiatric disorders (Abu-Akel and Shamay-Tsoory, 2011), and that social cognition, and thus mentalizing, appears to significantly influence functional outcomes in some disorders, such as schizophrenia, bipolar affective disorder, major depression (Velthorst et al., 2017).

Several meta-analyses have confirmed the presence of mentalizing deficits in schizophrenia (Sprong et al., 2007; Bora et al., 2009). In addition, differences in mentalizing functioning have been shown in first-degree asymptomatic relatives and high-risk individuals (Bora and Pantelis, 2013). Thus, as a result of this research, mentalization has emerged as a possible endophenotype, i.e., it is genetically determined, well measurable, present in the disease, independent of status, and also occurs in relatives (Martin et al., 2014). It should be noted, however, that research in this area is still in its early stages and results on heritability, among others, are not yet consistent. However according to our view, the results are significantly influenced by the mentalization paradigm used for the studies. Indeed, most studies have used tests that explicitly measure mentalization. Explicit mentalization, on the other hand, is significantly determined culturally/environmentally (Heyes and Frith, 2014). In contrast, implicit mentalization is presumably more biologically determined. It is a skill, which is probably present from birth, but it is more certain that it is an important skill in the preverbal period (Apperly and Butterfill, 2009; Vogeley, 2017). In this sense, implicit mentalizing is more proximal to the genetic, biological background compared to explicit mentalization, and therefore, the study of implicit mentalization would probably carry more information regarding genetic associations.

Our study has shown that implicit mentalization is also deficient in schizophrenia, but the quality of evidence is low, presumably due to the low number of cases and the highly heterogeneous study methods.

Based on these studies, and our meta-analysis, it can be assumed that the implicit dimension of mentalizing is a more appropriate endophenotype, as it is characterized by a complete lack of awareness, is non-verbal, is probably present from birth, is presumably more biologically determined than explicit mentalization, and may thus better reflect neurobiological etiological factors.



## **V. New results**

1 We first described the prevalence of MPA in first-degree asymptomatic relatives of patients with bipolar I affective disorder compared to controls. This suggests that MPA is a plausible endophenotype of bipolar I affective disorder.

2. We found a higher frequency of head and mouth region abnormalities in asymptomatic relatives of individuals with bipolar I affective disorder, which may indicate an early neurodevelopmental disorder.

3. We found a higher frequency of a minor malformation (sole crease) and a phenogenetic variant (high arched palate) in asymptomatic relatives of people with bipolar I affective disorder.

4 We are the first to demonstrate, based on the results of our systematic review and meta-analysis, that in schizophrenia, in addition to deficits in explicit mentalizing, implicit mentalizing performance is also deficient.

5. Implicit mentalizing performance of patients with schizophrenia is more inaccurate, reaction time is slower, brain activation activity is different, and visual scanning is different compared to control subjects.

## VI. Publications

### Publications on which the thesis is based

Csulak, T., Csábi, Gy., Herold, R., Vörös, V., Jeges, S., Hajnal, A., Kovács, M.Á., Simon, M., Herold, M., Tóth, Á.L., Tényi, T. (2021) Increased Prevalence of Minor Physical Anomalies Among the Healthy First-Degree Relatives of Bipolar I Patients - Results With the Méhes Scale. FRONTIERS IN PSYCHIATRY. Apr 29;12:672241. doi: 10.3389/fpsy.2021.672241. IF: 4,157

Csulak, T., Hajnal, A. S., Kiss, Sz., Dembrowszky, F., Varjú-Solymár, M., Sipos, Z., Kovács, M. Á., Herold, M., Varga, E., Hegyi, P., Tényi T., Herold R. (2022) Implicit mentalizing in patients with schizophrenia: a systematic review and meta-analysis FRONTIERS IN PSYCHOLOGY 13 Paper: 790494 , 11 p. IF: 2,990

### Publications related to the topic of the thesis

Csulak, T., Herold, R. (2021). Az implicit és spontán mentalizáció eltérései szkizofréniában. PSYCHIATRIA HUNGARICA, 36(1), 67–80.

Csulak, T., Varga, E., Tényi, T., Hajnal, A., Varga, J., Herold, R. (2020) Iróniamegértés a bipoláris affektív zavarban szenvedő betegek elsőfokú hozzátartozói esetében – pilot fMRI vizsgálat PSYCHIATRIA HUNGARICA 35(4):540-546.

Fekete, J., Pótó, Zs., Varga, E., Csulak, T., Zsélyi, O., Tényi, T., Herold, R. (2020) Persons With Schizophrenia Misread Hemingway: A New Approach to Study Theory of Mind in Schizophrenia. FRONTIERS IN PSYCHIATRY. May 7;11:396. doi: 10.3389/fpsy.2020.00396 IF: 4,157

### **Abstracts related to the thesis**

Csulak, T., Csábi, G., Herold, R., Hajnal, A., Kovács, M., Herold, M., Jeges, S., Tényi, T. (2021) Bipoláris I affektív zavarban szenvedő betegek egészséges elsőfokú hozzátartozóinak minor fizikális anomália vizsgálata. PSYCHIATRIA HUNGARICA, 36(Suppl. 1), 20–20.

Csulak, T., Hajnal, A., Tényi, T., Herold, M., Herold, R. (2021) Spontán és implicit mentalizáció szkizofrén betegek esetében. PSYCHIATRIA HUNGARICA, 36(Suppl. 1), 20–20.

Csulak, T., Varga, E., Tényi, T., Hajnal, A., Varga, J., Herold, R. (2021) Iróniamegértés a bipoláris affektív zavarban szenvedő betegek elsőfokú hozzátartozói esetében – pilot vizsgálat. PSYCHIATRIA HUNGARICA, 36(Suppl. 1), 21–21.

Hajnal, A., Varga, E., Csulak, T., Herold, R., Tényi, T. (2021) Minor fizikális anomáliák bipoláris zavarban. PSYCHIATRIA HUNGARICA, 36(Suppl. 1), 39–39.

### **Abstracts not related to the topic of the thesis**

Herold, M., Tényi, T., Csulak, T., Kovács, M., Hajnal, A., Herold, R. (2021) Az átmeneti tárgy használat és a szociális kogníció összefüggése borderline személyiségzavarban. PSYCHIATRIA HUNGARICA, 36(Suppl. 1), 44–44.

### **Other publications not related to the subject of the thesis**

Tényi, T., Csulak, T., Herold, M., Kovács, M. Á. (2021) „Praecox-Gefühl” – Rövid rátekintés. PSYCHIATRIA HUNGARICA, 36(4), 617–620.

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