



# The familiarity of Romanian psychiatrists with anti-N-methyl-D-aspartate receptor encephalitis: findings from a web-based survey study

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## Abstract

**Background and aims.** Psychiatrists are often the first to be consulted in patients with anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. Thus, they need to be aware of clinical features, differential diagnoses, and treatment options for this condition. In this study, we aimed to investigate the familiarity of Romanian psychiatrists with anti-NMDAR encephalitis.

**Methods.** We recruited psychiatrists from Romania and conducted a cross-sectional observational study by using a web-based survey.

**Results.** The survey was completed by 111 psychiatrists, of whom 47 (42.34%) were specialists, while 64 (57.66%) were trainees. The median length of training for specialists was ten years (interquartile range - IQR 9.5), while for trainees it was 2.5 years (IQR 3). In total, 31 (27.93%) psychiatrists encountered a case of anti-NMDAR encephalitis, with no significant difference between specialists and trainees. 31 (27.93%) psychiatrists were either unaware of the disorder or only knew its name, while 77 (69.37%) had knowledge of an outline of it. Only 3 (2.7%) psychiatrists had comprehensive knowledge of the disorder. Respondents with a higher awareness level had undergone significantly longer training ( $p=0.014$ ). Unsurprisingly, having encountered a case significantly influenced awareness levels ( $p<0.001$ ). There were no significant differences between specialists and trainees regarding specific knowledge about anti-NMDAR encephalitis. However, higher awareness levels and having encountered a case significantly influenced answer accuracy for questions regarding psychiatric presentation and epidemiological features.

**Conclusions.** Our study indicates that Romanian psychiatrists have suboptimal knowledge of anti-NMDAR encephalitis, highlighting the need for improved awareness of this disorder.

**Keywords:** anti-N-methyl-D-aspartate receptor encephalitis, psychiatrists, Romania, surveys and questionnaires

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### Background and aims

Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a neuroinflammatory disorder in which antibodies target and interfere with the function of the GluN1 subunit of the receptor [1]. It can be challenging to distinguish this condition from primary psychiatric disorders, as > 90% of patients present with psychotic symptoms, behavioral changes, or cognitive dysfunction [2]. As a result, up to 80% of patients initially consult a psychiatrist, while 40% are subsequently admitted to psychiatric wards [1].

Identifying and providing proper and rapid treatment for anti-NMDAR encephalitis is crucial. Failing to do so can lead to severe consequences. In the absence of treatment, 6% of patients die, and most experience residual cognitive deficits and behavioral problems. Approximately 15% of patients have relapses [2]. Thus, psychiatrists need to be aware of clinical features, differential diagnoses, and treatment options for patients affected by this condition [3].

According to some researchers, psychiatrists may have insufficient knowledge about anti-NMDAR encephalitis. However, the existing data are limited. Only two studies on this subject were conducted, one in 2012 [4] and another in 2015 [5]. Yet, the data might reflect geographic peculiarities as they were conducted in Japan and Australia, respectively. Therefore, it is not recommended to make broad generalizations based on these data alone.

In this study, we aimed to investigate the familiarity of Romanian psychiatrists with anti-NMDAR encephalitis. In the first step, we collected general information regarding professional status and overall medical experience. Then, we sought to assess the level of knowledge regarding specific basic, clinical, and therapeutic aspects of the disorder. To achieve these objectives, we created a web-based questionnaire distributed to a sample of Romanian psychiatrists.

### Methods

#### Study design

This cross-sectional observational study utilized a web-based survey created on Google Forms. Respondents were recruited over eight weeks (between October and December 2023) through an open-access link via mailing lists and social media platforms. We replicated a similar Japanese study [4] with written permission from the first author.

#### Subjects

To be included in the study, individuals had to (1) be a specialist or trainee in adult psychiatry and (2) be located or working in Romania. Individuals were excluded from the study if they (1) did not have a medical degree, or (2) had another specialty than Adult Psychiatry. Respondents were asked to read the electronic participant information sheet, which detailed the aims and scope of the study. Following

this, they were asked to provide consent. Respondents were informed that data would be collected anonymously and would not be tracked in any way. This study conformed with the World Medical Association Declaration of Helsinki and received approval from the Ethics Committee of the Iuliu Hațieganu University of Medicine in Cluj-Napoca, Romania (ref: AVZ248/28.09.2023).

#### Web-based survey

Questions were written in clear Romanian and were in the format of tick-boxes and free-text fields. The survey contained 12 items, of which three were general, while nine were specific. The general items referred to:

- 1) respondent's professional status: specialist or trainee,
- 2) year of graduation from medical school, and
- 3) number of years of training in Psychiatry.

The specific items referred to knowledge about anti-NMDAR encephalitis:

- 1) whether the respondent has encountered an anti-NMDAR encephalitis case,
- 2) self-evaluation of the level of familiarity with the disorder,
- 3) proportion of patients presenting with psychiatric symptoms,
- 4) etiology,
- 5) proportion of patients having an associated tumor,
- 6) the existence of a purely psychiatric presentation,
- 7) diagnosis confirmation,
- 8) group of patients mainly affected,
- 9) treatment.

#### Statistical analyses

We analyzed data using JASP version 0.18.1 (University of Amsterdam, Netherlands). We tested normality and equality of variance using the Shapiro-Wilk and Levene's tests, respectively. Quantitative variables were described by median and interquartile range (IQR), while qualitative variables were presented by frequencies. We compared quantitative data between groups using the Mann-Whitney U or Kruskal-Wallis tests. Post hoc analysis was performed using Dunn's test with Bonferroni's correction for multiple comparisons. We used the chi-square ( $\chi^2$ ) test to compare the frequencies of qualitative variables. A confidence interval of 95% and two-tailed p-values < 0.05 were considered significant for all analyses.

### Results

#### General information on respondents

One hundred and eleven (111) psychiatrists completed the survey, of whom 47 (42.34%) were specialists, while 64 (57.66%) were trainees. The median graduation year for the whole group was 2018 (IQR 8), while the median length of training was five years (IQR 6.5). Specialists graduated significantly earlier and had significantly longer training than trainees ( $p < .001$ ) (Table I).

**Table I.** General information on the 111 respondents of our survey study.

	Specialists	Trainees	U	p-value
N (%)	47 (42.34)	64 (57.66)		
Year of graduation from medical school	2011 (11.5)	2020.5 (4)	30	<.001
Years of training in Psychiatry	10 (9.5)	2.5 (3)	2985.5	<.001

**Table II.** Knowledge about anti-N-methyl-D-aspartate encephalitis in the 111 respondents of our survey study. Percentages in bold typeface refer to the correct responses. *Abbreviations: NMDA - N-methyl-D-aspartate; EEG - electroencephalography; CSF - cerebrospinal fluid.*

	Specialists (n=47)	Trainees (n=64)	$\chi^2$	p-value
Encountered a case	25.53%	29.69%	0.23	0.63
(Q1) With regard to anti-NMDA receptor encephalitis do you consider yourself as:				
a) aware of only the name of the disorder	a) 10.64%	a) 29.69%	6.52	0.089
b) having comprehensive knowledge of the disorder	b) 4.26%	b) 1.56%		
c) having knowledge of an outline of the disorder	c) 76.6%	c) 64.06%		
d) unaware of the disorder	d) 8.51%	d) 4.69%		
(Q2) The number of patients with this disorder who first present with prominent psychiatric symptoms falls in which of the following ranges:				
a) 0–30%	a) 29.79%	a) 42.19%	3.68	0.055
b) 30–60%	b) 29.79%	b) 34.38%		
c) > 60%	c) <b>40.43%</b>	c) <b>23.44%</b>		
(Q3) The etiology of the disorder is:				
a) <b>autoimmune</b>	a) <b>95.75%</b>	a) <b>90.63%</b>	1.06	0.303
b) infective	b) 2.13%	b) 1.56%		
c) unknown	c) 2.13%	c) 7.81%		
(Q4) Percentage of patients with this disorder who are found positive for an associated tumor:				
a) 0–30%	a) 51.06%	a) 48.44%	0.17	0.68
b) <b>30–60%</b>	b) <b>38.3%</b>	b) <b>42.19%</b>		
c) >75%	c) 10.64%	c) 9.38%		
d) 100%	d) 0%	d) 0%		
(Q5) A purely psychiatric presentation of the disorder has been described:				
a) <b>yes</b>	a) <b>70.21%</b>	a) <b>62.5%</b>	0.72	0.397
b) no	b) 29.79%	b) 37.5%		
(Q6) Diagnosis is confirmed on:				
a) brain imaging	a) 0%	a) 3.13%	0.1	0.749
b) EEG findings	b) 0%	b) 0%		
c) <b>paired serum and CSF testing</b>	c) <b>97.87%</b>	c) <b>96.88%</b>		
d) can only be made post-mortem	d) 2.13%	d) 0%		
(Q7) The disorder is most often described in:				
a) children	a) 2.13%	a) 6.25%	0.66	0.417
b) elderly females	b) 2.13%	b) 0%		
c) elderly males	c) 4.23%	c) 0%		
d) <b>females in 2<sup>nd</sup>–5<sup>th</sup> decades</b>	d) <b>76.6%</b>	d) <b>82.81%</b>		
e) males in 2 <sup>nd</sup> –5 <sup>th</sup> decades	e) 14.89%	e) 10.94%		
(Q8) The mainstay of treatment is:				
a) antibiotic treatment	a) 4.25%	a) 0%	2.77	0.096
b) <b>immunomodulation</b>	b) <b>95.75%</b>	b) <b>100%</b>		
c) antiviral treatment	c) 0%	c) 0%		

**Knowledge about anti-NMDAR encephalitis**

Table II presents information on the respondents' knowledge about the disease.

**Psychiatrists who encountered a case**

Out of 111 psychiatrists, 31 (27.93%) had encountered a case of anti-NMDAR encephalitis during

their practice. There were no significant differences in graduation year or length of training between those who encountered a case and those who had not. Moreover, having encountered a case was unrelated to whether the psychiatrist was a specialist or a trainee. However, trainees had a slightly higher proportion of individuals who

encountered a case (29.69% vs. 25.53%).

### Self-evaluated awareness of the disorder (Q1)

Out of 111 psychiatrists, 3 (2.7%) had “comprehensive knowledge of the disorder,” while 77 (69.37%) had “knowledge of an outline of the disorder.” On the other hand, 24 (21.62%) were “aware of only the name of the disorder,” while 7 (6.3%) were “unaware of the disorder.” There was no significant difference between specialists and trainees regarding the self-evaluation. However, awareness levels were significantly influenced by graduation year [ $H(2)=9.676$ ,  $p=0.022$ ] and length of training [ $H(2)=9.878$ ,  $p=0.02$ ]. Dunn’s post hoc tests showed that those with “knowledge of an outline of the disorder” graduated significantly earlier ( $p=0.003$ ) and had significantly longer training ( $p=0.002$ ) than those “aware of only the name of the disorder”. After Bonferroni’s correction, the significance was maintained ( $p=0.018$  and  $p=0.014$ , respectively). Moreover, encountering a case significantly influenced the self-evaluated awareness levels ( $\chi^2=19.14$ ,  $p<0.001$ ).

### Specific knowledge about anti-NMDAR encephalitis (Q2-Q8)

There was no significant difference in the rates of correct answers to Q2-Q8 between specialists and trainees. However, having encountered a case significantly influenced the accuracy of answers to Q4 ( $\chi^2=5.48$ ,  $p=0.019$ ) and Q7 ( $\chi^2=7.45$ ,  $p=0.006$ ). Likewise, the self-evaluated awareness levels significantly influenced the accuracy of answers to Q2 ( $\chi^2=9.02$ ,  $p=0.029$ ), Q4 ( $\chi^2=8.64$ ,  $p=0.035$ ), and Q7 ( $\chi^2=13.36$ ,  $p=0.004$ ).

## Discussion

This cross-sectional observational study indicates that knowledge of anti-NMDAR encephalitis among Romanian psychiatrists is suboptimal. Only about 30% of all respondents encountered a case during their clinical practice; slightly more trainees than specialists were present among these. Moreover, about 30% of the psychiatrists were either unaware of the disorder or only knew its name, while the majority had only knowledge of an outline of it. Only a tiny minority had comprehensive knowledge about the disorder. The respondents who had higher awareness levels had undergone significantly longer training. Furthermore, having encountered a case significantly influenced self-evaluated awareness levels. Regarding specific knowledge about anti-NMDAR encephalitis, there were no significant differences between specialists and trainees. However, higher awareness levels and having encountered a case significantly impacted the accuracy of answers to questions regarding psychiatric presentation and epidemiological features.

The psychiatric community has become increasingly aware of anti-NMDAR encephalitis since it was first described in 2007 [6]. However, the few studies conducted so far showed that knowledge of the disorder among psychiatrists was inadequate. The Japanese study

[4] conducted in 2012 showed that only 9.2% of the respondents had encountered an anti-NMDAR encephalitis case. The percentage increased to 16.87% of specialists and 13.95% of trainees in the Australian study [5] conducted in 2015. Although our study revealed a further rise to 25.53% in specialists and 29.69% in trainees, it still indicates a suboptimal situation. These observed serial increments are likely due to an increase in awareness of the disorder [7], leading to more extensive neural antibody testing in psychiatric patients rather than an increase in incidence.

As the number of psychiatrists encountering anti-NMDAR encephalitis cases increased over the years, their familiarity with the condition also grew. In the Japanese study [4], psychiatrists “having knowledge of an outline of the disorder” comprised 21% of respondents. The percentage increased to 42.53% in specialists and 51.16% in trainees in the Australian study [5]. Our study showed a further rise to 76.6% in specialists and 64.06% in trainees. Furthermore, we observed that Romanian psychiatrists with a higher awareness level had undergone significantly longer training. These data contrast those from the Japanese study [4], where psychiatrists “having knowledge of an outline of the disorder” had a significantly shorter tenure than the others. These diverging observations could mean that Romanian psychiatrists rely more on training in acquiring knowledge than their Japanese counterparts. In line with this explanation, having encountered a case significantly influenced awareness levels in our group as well. While there is a clear positive trend, 27.92% of all Romanian respondents were still “unaware of the disorder” or “aware of only the name” of it.

We did not observe significant differences between the accuracy of specialists and trainees regarding specific questions about anti-NMDAR encephalitis (Q2-Q8). Yet, higher awareness levels and having encountered a case significantly influenced the accuracy of answers to questions regarding psychiatric presentation and epidemiological features (Q2, Q4, and Q7). There were noteworthy differences between the accuracy of Romanian psychiatrists and their Australian counterparts [5] regarding Q2 and Q5. One must remember that the two studies were conducted eight years apart, reflecting a lag in knowledge acquisition for Romanian psychiatrists. The low accuracy for Q2 and Q5 is concerning, given that >90% of patients with anti-NMDAR encephalitis present with psychiatric symptoms, and up to 80% initially consult a psychiatrist [1,2]. Usually, neurological complications follow the initial psychiatric phase, aiding in reaching the diagnosis [8]. However, about 4% of patients do not advance to the neurological phase and remain purely psychiatric [9]. Romanian psychiatrists might miss patients with anti-NMDAR encephalitis in the early phase due to being less aware of these peculiarities. Moreover, we observed low accuracy for Q4 as well. About 40% of patients, primarily females aged 12-45, have an underlying tumor, usually ovarian teratomas [10]. A low

awareness of this association could lead to worse outcomes, as tumor removal is an essential therapeutic option [8].

This study has a few strengths. It is the first study of its kind in Romania and, to our knowledge, in Europe. It remains to be determined if the findings are due to population peculiarities, as previous studies were conducted in Japan [4] and Australia [5]. Also, our study provides an updated perspective, given that previous studies were conducted in 2012 and 2015, respectively.

Nonetheless, there are significant limitations that must be taken into consideration as well. Firstly, the responses to the questionnaire were self-reported and may not accurately reflect the objective level of knowledge among respondents. Secondly, the sample was relatively small, although larger than the one reported by the Japanese study [4]. Thirdly, participants were recruited through mailing lists and social media, which may not be representative of the entire population. Moreover, the sample was demographically heterogeneous as less than half of the respondents were licensed psychiatrists. It is unclear whether these findings can be generalized to the entire population and, therefore, may not accurately reflect the knowledge levels of Romanian psychiatrists.

### Conclusions

Our study indicates that Romanian psychiatrists have suboptimal knowledge of anti-NMDAR encephalitis, with gaps in critical areas such as psychiatric presentation and epidemiological features. These findings highlight the importance of improving Romanian psychiatrists' awareness of anti-NMDAR encephalitis.

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