**Original Article**

# Noise pareidolia test for predicting delirium in hospitalized older patients with cognitive decline

Yutaka Hashimoto,[1,3] Osamu Kano,[2] Satoru Ebihara[1,4*]

[1] Department of Rehabilitation Medicine, Toho University Graduate School of Medicine, Tokyo, Japan

[2] Department of Neurology, Toho University Faculty of Medicine, Tokyo, Japan

[3] Department of Geriatric Nursing, Toho University Faculty of Nursing, Tokyo, Japan

[4] Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, Japan

**Running title**: Prediction of delirium by pareidolia

* Correspondence to:

Satoru Ebihara, MD, PhD

Department of Internal Medicine and Rehabilitation Science

Tohoku University Graduate School of Medicine

1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan

Tel +81-22-717-7353

Fax +81-22-717-7355

E-mail: satoru.ebihara.c4@tohoku.ac.jp

**ABSTRACT**

**Aim:** Although older people are at an increased risk of developing delirium during hospitalization, no definitive screening tools exist to predict the condition. This study aimed to examine the effectiveness of the noise pareidolia test (NPT) as a tool for predicting the onset of post-hospitalization delirium in older adults.

**Methods:** Hospitalized patients who were cared for by a multidisciplinary geriatric care team due to behavioral symptoms, difficulties in communication, and a history of dementia or delirium were analyzed. The NPT was performed on patients who could complete a Mini-Mental State Examination within 3 days of admission. Demographic and clinical data were recorded on the same day as the NPT or within 3 days of admission. Delirium was assessed using the observation-based Delirium Screening Tool (DST).

**Results:** Of the 96 patients, 59 were in the DST-negative group and 37 in the DST-positive group. Benzodiazepine (BZD) agonist use, serum potassium (K) levels, and the number of images in which pareidolia was noted (i.e., the NPT score) significantly differed between the groups. Logistic regression analysis identified BZD agonist use (odds ratio, 2.897; $P$=0.032), serum K levels (odds ratio, 0.427; $P$=0.041), and NPT scores (odds ratio, 1.253; $P$=0.017) as significant predictors of DST results. The receiver operating characteristic curve analysis showed an NPT score of 1 as the appropriate cutoff value.

**Conclusions:** A positive NPT score was identified as an independent predictor of delirium in older patients admitted to an acute care hospital with cognitive dysfunction.

**Key words:** Cognitive decline, Delirium, Hospitalization, Older patients, Pareidolia

## INTRODUCTION

Current advances in medical technology have improved the quality of life for many older adults undergoing medical treatments. The number of older patients admitted to acute care hospitals has also increased, presenting the challenge of delirium onset in these hospitalized patients. The incidence of delirium is 18–35% in all patients[1] and 25–40% in in-patients aged ≥65 years.[2] The incidence of delirium in hospitalized older patients increases from 5.1% to 52.2% with the increase in age.[3]

Although older patients requiring hospitalization for underlying diseases may be at an increased risk of developing delirium due to the hospitalization itself, it is difficult to diagnose delirium using neurological, physical, and imaging examinations.[4] A reliable screening tool for assessing delirium and determining its severity must complement insights provided by medical histories and physical examinations. Currently, there is no reliable method to predict delirium.

Pareidolia is a psychological phenomenon in which an individual recalls familiar patterns upon receiving visual and auditory stimuli despite such patterns not existing in the patient's environment. Visual pareidolia, with reports such as "stains on the wall look like insects" and "curtains and shadows look like humans," is a typical symptom of delirium[5] and Lewy body dementia,[6] which share several characteristics.[7] The noise pareidolia test (NPT) effectively diagnoses Lewy body dementia. The NPT is also potentially applicable in diagnosing delirium, which similarly involves visual hallucinations and may be a useful predictor of delirium. However, there is a lack of literature on the topic, with only one study on delirium and pareidolia by Maeda et al., suggesting that the presence of pareidolia may be a risk factor for postoperative delirium in older people.[8]

The NPT was developed by Yokoi et al. to assess visual pareidolia quantitatively.[9,10] Our study aimed to examine whether the NPT can be used to predict the onset of post-hospitalization delirium in older patients.

## METHODS

### *Participants*

This study evaluated patients aged ≥65 admitted to the Toho University Medical Center Omori Hospital between February 2020 and June 2021 and cared for by a multidisciplinary geriatric medical care team. The intervention criteria for the geriatric care team were as follows: 1) age ≥65 years with behavioral symptoms, communication difficulties, or cognitive declines that may have interfered with their daily lives and were noted in pre-hospital screenings; 2) a history of dementia; 3) taking anti-dementia drugs; or 4) a history of delirium. All patients that satisfied these conditions were cared for by the geriatric care team of the hospital unless they were discharged within two days.

The exclusion criteria were as follows: 1) inability to undergo the Mini-Mental State Examination Japanese (MMSE-J)[11]; 2) inability to perform the NPT due to cognitive dysfunction or visual or hearing problems; and 3) development of delirium before the NPT was carried out.

This study was approved by the Ethics Committee of Toho University Omori Medical Center (approval numbers M19138 and M21220). Written informed consent for participation was obtained from all patients or their representatives before enrollment in the study.

### *Research protocol*

The NPT was performed on patients who could complete the MMSE-J within 3 days of admission. Demographic and clinical data, such as sex, age, height, weight, body mass index (BMI), hospitalization type, presence/absence of dementia, presence/absence of anti-dementia drug intake, presence/absence of benzodiazepine (BZD) receptor agonist use, presence/absence of orexin receptor antagonist use, and presence/absence of polypharmacy (number of medications ≥6), were recorded. Blood test results, including serum albumin (Alb), sodium (Na), potassium (K), and chloride (Cl) levels, and the Geriatric Nutritional Risk Index (GNRI)[12] were collected from patient medical records on the same day as the NPT or within 3 days of

admission.

***NPT***

The NPT,[9,10] an improved version of the pareidolia test,[6] was conducted within 3 days of admission on those who could undergo the MMSE-J. A practice task was performed in which a doctor or nurse presented three noise images to a patient and asked whether they saw a face. The actual task was performed upon confirmation that the patient understood the practice task. For the actual task, 40 noise images were shown one by one for up to 30 seconds each, and the patient was instructed to respond to each. Pareidolia was considered if the patient reported a face in a noise image without a face or if they reported a face in an area of a noise image that was different from where the face was located in the image. The number of images for which pareidolia was noted (i.e., the NPT score) was recorded.

***Assessment of delirium***

Delirium was assessed using the Delirium Screening Tool (DST), a tool developed by Machida et al.[13] based on the Delirium Rating Scale (DRS) developed by Trzepacz et al.[14] The DST can easily be performed within 5 minutes, has a sensitivity of 98%, and has been verified as a useful screening tool. It is an observation-based delirium assessment tool consisting of three items: A) level of consciousness, arousal, and environmental awareness; B) change in cognition; and C) change in symptoms.

The DST was implemented as follows: a doctor or nurse evaluated all seven aspects of item A, including a sense of reality, decrease in activity, excitement, mood fluctuation, sleep-awakening level, delusion, and hallucination, scoring them as [Yes] or [No] based on patient examination and medical records. If at least one part of item A was evaluated as [Yes], both parts of item B, disorientation and memory disorder, were similarly evaluated as [Yes] or [No]. If at least one part of item B was evaluated as [Yes], both parts of item C, current mental state onset pattern and symptom fluctuation, were evaluated as [Yes] or [No]. If at least one part of

item C was evaluated as [Yes], the examiner determined that the patient was DST-positive, and the presence of delirium was possible. If all parts of item A were evaluated as [No], the examiner determined that the patient was DST-negative and did not have delirium.

The DST was used as a delirium evaluation index for 7 consecutive days after the NPT to determine whether a patient was DST-negative or positive based on medical records. If a patient was discharged within 7 days after the NPT, the number of days until discharge was noted.

***Statistical analysis***

The DST-negative and DST-positive groups were compared in terms of sex, hospitalization type, dementia diagnosis, anti-dementia drug use, BZD receptor agonist use, orexin receptor antagonist use, and polypharmacy using the $\chi^2$ test. Age; BMI; GNRI; serum Alb, Na, K, and Cl levels; MMSE-J; and NPT scores were compared using the Mann–Whitney U test. A binomial logistic regression analysis was performed that included statistically significantly different variables ($P<0.05$) between the two groups. These variables were set as independent variables, while the DST results were set as dependent variables. Serum K level, BZD receptor agonist use, and NPT score were used to create a delirium prediction index. With DST results set as the dependent variable, a receiver operating characteristic (ROC) curve analyzed the cutoff score to predict a positive DST result based on serum K levels, BZD receptor agonist use, and NPT score. IBM SPSS Ver. 26 statistics (SPSS Inc., Chicago, IL, USA) was used for statistical analyses, and the significance level was set to 5%.

**RESULTS**

Of the 118 patients who consented to the study, 22 were excluded from the analysis. Of these, 17 patients could not finish the NPT due to endurance and concentration problems, 3 could not undergo the test due to poor visual acuity, and 2 had delirium before the test. The 22

patients excluded from the analysis included one patient diagnosed with Lewy body dementia who was excluded due to the inability to understand the NPT (Figure 1). No participants withdrew consent during the study.

Ninety-six patients were analyzed, of whom 59 were DST-negative, and 37 were DST-positive (positivity rate=38.4%). The average patient age was 83.2 ± 5.9 years, the average MMSE-J score was 18.2 ± 4.8 points, and the average number of images for which pareidolia was noted in the NPT was 2.3 ± 3.1. Thirty-three patients were diagnosed with dementia, with the following classifications: 32 patients had Alzheimer's disease, 1 had vascular dementia (VaD), and the remaining 63 had no definite diagnosis. One of the patients in the initial group had Lewy body dementia but was excluded from the test because of the inability to understand it.

A $\chi^2$ test was performed to compare sex, hospitalization type, dementia diagnosis, anti-dementia drug use, BZD receptor agonist use, orexin receptor antagonist use, and multidrug administration. Results indicated that BZD receptor agonist use was significantly higher in the DST-positive group than in the DST-negative group ($P$=0.023) (Table 1). Age; BMI; GNRI; serum Alb, Na, K, and Cl levels; MMSE-J total score; and NPT scores were compared between the two groups using the Mann–Whitney U test. Results showed that serum K was significantly lower, and NTP scores were significantly higher in the DST-positive group than those in the DST-negative group ($P$=0.030 and $P$<0.001, respectively) (Table 1).

Based on the results of the $\chi^2$ test and Mann–Whitney U test, a binomial logistic regression analysis was performed with the DST-negative and DST-positive groups as dependent variables, and the presence or absence of BZD receptor agonist use, serum K level, and NPT scores as independent variables. Presence or absence of BZD receptor agonist use (odds ratio 2.897; 95% confidence interval (CI): 1.097–7.616; $P$=0.032), the fluctuation of serum K levels (odds ratio 0.427; 95% CI: 0.189–0.965; $P$=0.041), and the fluctuation of NPT scores (odds ratio 1.253; 95% CI: 1.042–1.508; $P$=0.017) were identified as significant variables (Table 2).

With the DST-negative and DST-positive groups set as dependent variables, an ROC curve was drawn to examine the cutoff value for determining the possibility of DST being positive based on NPT score, BZD receptor agonist use, and serum K level. The areas under the ROC curve (AUC) were as follows: NPT = 0.737 (95% CI: 0.634−0.839), BZD = 0.611 (95% CI: 0.493−0.729), and serum K = 0.363 (95% CI interval: 0.253−0.483); a convex curve was drawn toward the upper left. When the cutoff value was determined from the ROC curve, a total NPT score of 1, BZD agonist use, and a serum K level of 4.0 were shown to be appropriate. The sensitivities of NPT score, BZD agonist use, and serum K level were 83.8%, 45.9%, and 35.1%, respectively, while the corresponding specificities were 59.3%, 76.3%, and 35.6%, respectively (Figure 2).

## DISCUSSION

This study aimed to examine whether the NPT could serve as a predictive indicator of new-onset delirium in older in-patients with cognitive decline. The results suggest that the NPT is a promising risk assessment and prediction method.

The older hospitalized patients with cognitive dysfunction had a post-hospitalization DST-positive rate of 38.4%, consistent with previous results.[1,2] Since this study only assessed older patients with cognitive dysfunction, comparisons regarding the incidence of delirium with older patients without cognitive dysfunction may not be possible. Older people with dementia are 5.2 times more likely to have delirium than those without dementia.[15] Advanced age and cognitive dysfunction are considered major risk factors for the onset of delirium. The present study showed no significant difference in age between the DST-positive and -negative groups. Older people are at an increased risk of delirium.[16] Since the recruited patients had cognitive decline, the results of this study suggest that cognitive dysfunction may be a more important factor in the onset of delirium than advanced age.

There was a significant difference in the use of BZD receptor agonists between the

groups. Older people take BZD receptor agonists daily,[17] but improper use increases the risk of falls and delirium.[18] Therefore, guidelines for the proper use of drugs in the older population recommend refraining from BZD receptor agonist use.[19] The results of the present study support this literature.

Lipowski classified delirium-related factors as direct, inducing, and preparatory factors.[20] The onset of delirium is caused by a complex combination of these three factors that cause hyperexcitability and hypoactivity in the brain.[21] We examined an inducing factor, the type of hospitalization (emergency or scheduled); however, it did not affect DST positivity. We believe that environmental change such as hospitalization may be a factor in the onset of delirium for older people rather than hospitalization type.

There were no significant differences between the groups in MMSE-J scores, dementia diagnosis, or anti-dementia drug use (Table 1). The average MMSE-J score was 18.2 ± 4.8 points. Utilizing multiple cognitive domains is necessary for complex decision-making, which becomes difficult when MMSE scores are 19 points or less.[22] Since the NPT used in this study did not utilize multiple cognitive domains like decision-making, we believed an MMSE-J score of 18 points was sufficient as an index to gain an understanding of the test. The NPT and the MMSE-J combination is important for improving the accuracy of the NPT.

A significant difference was found in the total NPT score between groups, indicating that pareidolia was present in the DST-positive group. The NPT has been used as a diagnostic tool for Lewy body dementia.[9,10] Perceptual disturbances, with reports such as "stains on the wall look like insects" and "curtains and shadows look like humans," are typical symptoms of delirium observed in 70.2% of patients at the onset of delirium.[5] Delirium and Lewy body dementia also share many characteristics.[7] The results of the present study indicate that pareidolia may be a useful predictive tool for delirium as for Lewy body dementia. When pareidolia is detected by the NPT, the positive rate of DST increases, suggesting that it is an effective testing method for predicting the onset of delirium.

Previous studies have reported that electrolyte disorders (particularly hyponatremia)

and malnutrition are risk factors for delirium and postoperative delirium.[23,24] In the present study, the DST-positive rate increased as the serum K level decreased. It is possible that hypokalemia prevented the maintenance of intracellular volume, rapidly destroying the balance in osmolality and resulting in fluid abnormalities such as dehydration.[25,26] Therefore, maintaining serum K and other electrolytes balance is important for preventing delirium.

Since the AUC of the ROC curve was ≥0.7 (Figure 2), it can be expected that the total NPT score has sufficient discriminating ability concerning the presence or absence of DST. If the total NPT score of 1 was set as the cutoff value, the sensitivity and specificity of distinguishing DST positivity were 83.8% and 59.3%, respectively, suggesting that the NPT is effective in predicting delirium. However, the NPT is not sufficient by itself. Care interventions such as environmental adjustments, comprehensive assessments of the need for BZD receptor agonist use, and follow-ups on blood test results are important.

The limitation of this study was that the onset of delirium was determined using the DST, a screening tool that requires the judgment of a psychiatrist to diagnose delirium. The DST was created based on the DRS, which is widely used and highly reliable as an evaluation tool for delirium.[14] The DST has also received high praise from Trzepacz, the creator of the DRS.[13] Hence, a positive DST result may at least indicate that delirium is likely to have developed. One limitation of this study is that of the 96 patients analyzed in the present study, 32 were diagnosed with Alzheimer's disease, while 1 had VaD. Another patient had Lewy body dementia but was excluded from analysis due to the inability to understand the NPT. The remaining 63 patients, who had not been diagnosed with dementia, are highly likely to have had dementia despite the absence of a diagnosis, based on the intervention criteria. The prevalence of Alzheimer's disease, VaD, and Lewy body dementia (i.e., dementia subtypes) in Japan is 67.8%, 11.4%, and 4.8%, respectively[27]; thus, some of the above 63 patients may have had Lewy body dementia. The difficulty in diagnosing Lewy body dementia raises the possibility that it was present but was undetected among the 33 patients diagnosed with Alzheimer's disease. Based on a previous study that reported that 15% of patients with

Alzheimer's disease and 32% of patients with Lewy body dementia had experienced delirium,[28] the possibility that Lewy body disease was present in a certain number of DST-positive patients in the present study cannot be ruled out. In light of a previous finding that an extremely high proportion (61.3%) of patients with Lewy body dementia have a positive NPT score,[29] if such patients were present, the results of the present study may have overestimated the effect of the NPT in its use during hospitalization to predict delirium among older patients with dementia.

In conclusion, a positive NPT score was an independent predictor of delirium development in older patients admitted to an acute care hospital with cognitive dysfunction. Further examination of whether the NPT is effective in predicting the onset of delirium in older people who do not have cognitive dysfunction may be needed.

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**Disclosure statement**

The authors declare no conflicts of interest in association with the present study.

**Author contributions**

YH wrote the manuscript and analyzed the data. OK and SE designed and supervised the research.

**Data availability statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request**.**

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## FIGURE LEGENDS

### Figure 1

Flowchart depicting participant enrollment.

### Figure 2

Solid line: Receiver operating characteristic (ROC) curve for noise pareidolia test (NPT) score. The area under the curve (AUC) of the ROC curve was 0.737, and a convex curve was drawn toward the upper left. When the cutoff value of the NPT was 1, the sensitivity was 83.8%, and the specificity was 59.3%.

Dashed line: Receiver operating characteristic (ROC) curve for benzodiazepine (BZD) receptor agonist use. The area under the curve (AUC) of the ROC curve was 0.611, and a convex curve was drawn toward the upper left. When the cutoff value of the BZD was 1, the sensitivity was 45.9%, and the specificity was 76.3%.

Dash-dot-dash line: Receiver operating characteristic (ROC) curve for serum K. The area under the curve (AUC) of the ROC curve was 0.368, and a convex curve was drawn toward the upper left. When the cutoff value of the serum K was 4.0, the sensitivity was 35.1%, and the specificity was 35.6%.

**Table 1.** Comparison of characteristics between the DST negative and positive groups (n=96)

| | DST negative (n=59) | DST positive (n=37) | *P*-value |
|---|---|---|---|
| Sex (female/male) | 37/22 | 24/13 | 0.831 |
| Type of hospitalization (emergency/scheduled) | 36/23 | 27/10 | 0.230 |
| Diagnosis of dementia, n | 23 | 13 | 0.705 |
| Antidementia drug use, n | 20 | 7 | 0.112 |
| BZD receptor agonist use, n | 13 | 18 | 0.023 |
| Orexin receptor antagonist, n | 11 | 5 | 0.512 |
| Polypharmacy, n | 46 | 32 | 0.298 |
| Age (years), mean (SD) | 83.4 (6.2) | 82.9 (5.5) | 0.621 |
| BMI ($kg/m^2$), mean (SD) | 20.4 (4.0) | 20.6 (4.6) | 0.633 |
| GNRI, mean (SD) | 84.2 (13.4) | 81.0 (13.8) | 0.294 |
| Serum Alb (g/dl), mean (SD) | 3.0 (0.6) | 2.8 (0.7) | 0.118 |
| Serum Na (mEq/l), mean (SD) | 137.9 (5.4) | 139.3 (4.6) | 0.346 |
| Serum K (mEq/L), mean (SD) | 4.1 (0.6) | 3.8 (0.5) | 0.030 |
| Serum Cl (mEq/L), mean (SD) | 102.5 (13.2) | 104.8 (5.4) | 0.499 |
| MMSE-J, mean (SD) | 18.1 (4.2) | 18.4 (5.6) | 0.973 |
| NPT score, mean (SD) | 1.5 (2.6) | 3.5 (3.3) | <0.001 |

DST: Delirium Screening Tool, BMI: body mass index, BZD: Benzodiazepine, GNRI: Geriatric Nutritional Risk Index, MMSE-J: Mini Mental State Examination-Japanese, Alb: albumin, NPT score: the number of images for which pareidolia was noted in the Noise Pareidolia Test (NPT)

Sex, type of hospitalization, diagnosis of dementia, anti-dementia drug, benzodiazepine receptor agonist use, orexin receptor antagonist use, and polypharmacy were analyzed by

the $\chi^2$test. Age, BMI, GNRI, serum Alb, serum Na, serum K, serum Cl, MMSE-J, and NPT score were analyzed by the Mann–Whitney U test.

**Table 2.** Logistic regression analysis with DST positivity as the dependent variable (n=96)

| Variable | *P*-value | Odds ratio | 95% confidence interval | |
|---|---|---|---|---|
| | | | Lower limit | Upper limit |
| BZD receptor agonist use | 0.032 | 2.897 | 1.097 | 7.616 |
| Serum K | 0.041 | 0.427 | 0.189 | 0.965 |
| NPT score | 0.017 | 1.253 | 1.042 | 1.508 |

DST: Delirium Screening Tool, BZD: benzodiazepine, NPT score: the number of images for which pareidolia was noted in the Noise Pareidolia Test.

Dependent variable: DST negative=0, DST positive =1

Figure 1

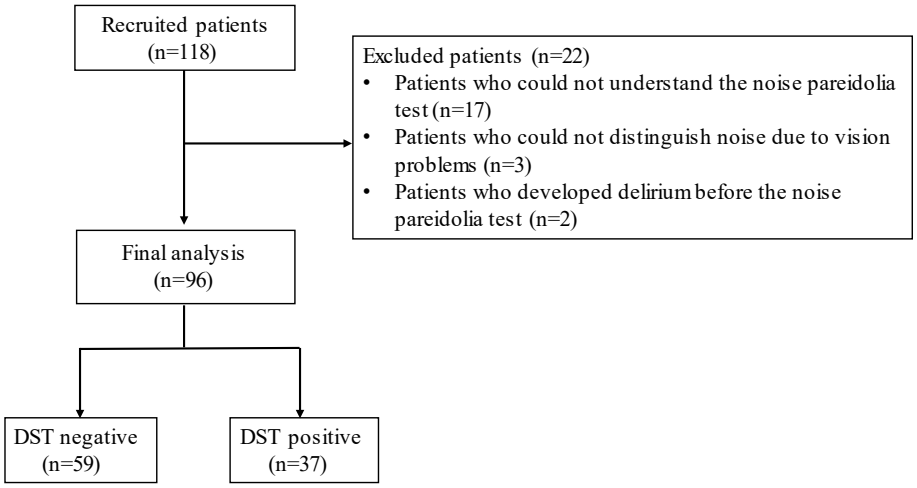
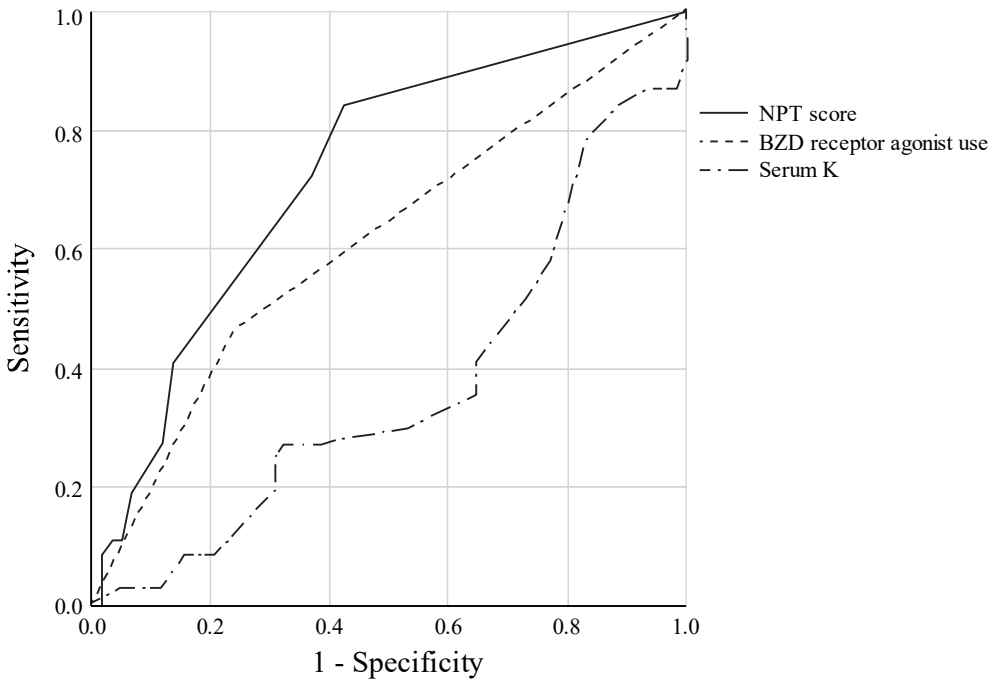

Recruited patients
(n=118)
Excluded patients (n=22)
• Patients who could not understand the noise pareidolia test (n=17)
• Patients who could not distinguish noise due to vision problems (n=3)
• Patients who developed delirium before the noise pareidolia test (n=2)
Final analysis
(n=96)
DST negative
(n=59)
DST positive
(n=37)

Figure 2


1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1 - Specificity
NPT score
BZD receptor agonist use
Serum K