Paroxysmal perceptual alteration (PPA) is the occurrence of brief and recurrent episodes of perceptual changes. It is mainly caused by the treatment of schizophrenia patients with antipsychotics. However, diagnosis of PPA is not very prevalent among psychiatrists, partly due to underrecognition or misunderstanding that it is a worsening of psychiatric symptoms. If psychiatrists do not understand PPA, they cannot treat it appropriately, and the patient’s quality of life is impaired. We present a case of PPA in catatonic schizophrenia that was successfully treated by switching to aripiprazole from risperidone. We suggest that the disappearance of PPA in our case was due to both discontinuing risperidone, which completely blocks D2 receptors, and replacing it with aripiprazole, which is characterized as a partial agonist of D2 receptors. Treatment of PPA will improve medication adherence and quality of life. It is important to recognize PPA as a possible side effect of treatment with antipsychotics.

### Abstract

Paroxysmal perceptual alteration (PPA) is the occurrence of brief and recurrent episodes of perceptual changes. It is mainly caused by the treatment of schizophrenia patients with antipsychotics. However, diagnosis of PPA is not very prevalent among psychiatrists, partly due to underrecognition or misunderstanding that it is a worsening of psychiatric symptoms. If psychiatrists do not understand PPA, they cannot treat it appropriately, and the patient’s quality of life is impaired. We present a case of PPA in catatonic schizophrenia that was successfully treated by switching to aripiprazole from risperidone. We suggest that the disappearance of PPA in our case was due to both discontinuing risperidone, which completely blocks D2 receptors, and replacing it with aripiprazole, which is characterized as a partial agonist of D2 receptors. Treatment of PPA will improve medication adherence and quality of life. It is important to recognize PPA as a possible side effect of treatment with antipsychotics.

### Key Words:
- Paroxysmal Perceptual Alteration
- PPA
- Schizophrenia
- Aripiprazole
- Partial Agonist
- Risperidone
- Antipsychotics
P帕氏症候群（PPA）的诊断需综合症状表现模式及临床症状（如知觉障碍、精神症状、自主症状、运动症状）。帕氏症候群的严重性已报告与抗精神病药物的递增剂量相关，且使用抗胆碱能药物可减轻（5,6）。眼肌痉挛危机被报告在PPA发作期间频繁出现（36.4%）（4）。

在一项针对388名接受抗精神病药物治疗的患者的研究中，PPA的发病率被报道为3.25%；此外，使用高 potency抗精神病药物（3.91%）的患者报告的发病率高于中-低 potency抗精神病药物（1.16%）（4）。此外，有报告称PPA伴随的第二代抗精神病药物，尤其是利培酮（7），最近被发表（7-13）。

我们报告了一例因暴露于利培酮而出现PPA，并在换用阿立哌唑后改善的病例。尚无研究表明PPA在特定精神分裂症亚型中的发病率更高，也不清楚PPA是否在精神分裂症中更常见于有明显阳性症状或更多负性症状的患者。然而，在我们的病例中，患者表示即使有症状，但未提及他有明显阳性的症状。我们认为需要进一步研究PPA。

**Case Presentation**

患者为30岁男性，有12年的周期性精神病发作病史。精神分裂症的诊断是根据ICD-10。他处于静止、无动性状态，对外界刺激没有反应。抗精神病药物治疗，如使用盐酸氟哌啶醇3 mg/日或盐酸利培酮6 mg/日被开始。当他受到某些测试或佛教纪念活动的刺激时，他无法饮食并服药。他被转入我们的医院，处于静止状态。入院检查，他凝视着空虚，不能说话。肌肉紧张度增加，僵直是存在的。他的生命体征，如体温和血压，都是正常的，也没有出现自主性波动。所有实验室数据均在正常范围内，如肌酸激酶（CPK）水平为77 IU/l，C反应蛋白（CRP）为0.2 mg/dL，性传播疾病检测结果为阴性，并排除了神经变性综合征。他没有任何用药或饮酒史。脑电图显示正常，α-阻断试验呈阳性。磁共振成像（MRI）也未显示异常。单光子发射断层成像（SPECT）显示双侧额叶的血流灌注减少，这在精神分裂症中是常见的。他的阳性与阴性综合症量表（PANSS）得分为阳性因子（PANSS-P）35，阴性因子（PANSS-N）42，一般心理病理学因子（PANSS-G）95。虽然我们通过静脉注射盐酸氟哌啶醇10 mg/日和口服盐酸利培酮6 mg/日治疗，他的静止状态没有改善。因此，我们选择了电痉挛治疗（ECT）。ECT是双侧的，并使用肌肉松弛剂。每次ECT的发作时间约为40秒。在第五次ECT后，他的静止状态改善。我们停止了静脉注射盐酸氟哌啶醇，因为他说他可以口服药物，并将盐酸利培酮减到4 mg/日，尽管这低于精神分裂症的推荐剂量，因为他抱怨利培酮的副作用。他的PANSS-P得分改善到18，从35。然而，他的阴性症状，如动机下降，仍然严重；他的PANSS-N得分为40，PANSS-G得分为80，他整日躺在床上。当我们将他的一些症状详细地描述给他时，他说道，“我有时会感到和看到一切比正常情况下更大更近，然后我的思想就停止了。我感到害怕，因为我觉得我的身体可能会变硬。当我有这种感觉时，我就会躺在床上，这些症状会在几分钟内消失。”

我们诊断了这些症状为PPA，并决定换用阿立哌唑，因为它是对D2受体的半激动剂，我们以为PPA是由利培
peridone. Therefore, his treatment was changed from risperidone 4 mg/day to aripiprazole 18 mg/day. One week after changing to aripiprazole alone, his PPA had disappeared and his motivation was improved. His PANSS-P score was 16, PANSS-N was 19, PANSS-G was 34. As a result, the patient was discharged on aripiprazole after three weeks of treatment with it.

**Based on this hypothesis, it is possible that aripiprazole, which is characterized by partial agonism of D2 receptors, ameliorates PPA and risperidone worsens it.**

One year after discharge, the clinical improvement was maintained, and there is no worsening of psychiatric symptoms or PPA. His PANSS-P score is 11, PANSS-N is 12, and PANSS-G is 22. Because he is able to watch soccer on TV and go out alone, his quality of life has improved dramatically. The changes in the PANSS scores are shown in Table 1.

**Discussion**

PPA is characterized by paroxysmal hypersensitivity of perception, psychedelic experiences, and somatic schema disorder. In patients with chronic schizophrenia, PPA occurs abruptly, mainly in the evening, often precipitated by fatigue. During the attack, patients also suffer from mood and thought alterations, but they are aware that symptoms of PPA are not real and are not apprehensive about them. The attack ceases gradually and spontaneously while the patient rests or sleeps. These clinical features are clearly different from those of schizophrenic hallucinations (1).

One hypothesis of the pathophysiological mechanism of PPA was suggested by Watanabe (7, 14). Treatment of schizophrenia with antipsychotics causes dopaminergic dysfunction of the midbrain cortex, midbrain limbic cortex, and chronic block of D2 receptors (7, 14). When circadian variations of dopaminergic activity are added to these changes, acute dopaminergic activity decreases. As a result, increased noradrenergic activity (compensatory) causes hyperarousal, mood disorder (anxiety, agitation), hyperesthesia, and perceptual alteration. On the other hand, relatively increased acetylcholinergic activity causes thought disorder, mood disorder (depression), and motor symptoms (dystonia) (7, 14). Based on this hypothesis, it is possible that aripiprazole, which is characterized by partial agonism of D2 receptors, ameliorates PPA and risperidone worsens it.

Suggested treatments for PPA include reducing the dosage of antipsychotics (15), adding anticholinergic agents (5, 6), switching to antipsychotics with a transient and loose binding affinity for D2 receptors (10, 12), and administration of a β-blocker or benzodiazepines (14). Thus, aripiprazole might be effective because it maintains the dopaminergic nervous system in a steady state by partial agonism of D2 receptors (16). In our case, although switching medication carried the risk of worsening the patient’s positive symptoms, we chose aripiprazole, which is characterized by partial D2 receptor agonism and less sedation, because he complained of sleepiness. We diagnosed his symptoms as PPA caused by risperidone.

We suggest that the disappearance of PPA in our case was due to both completely stopping risperidone, which reduced the blockade of D2 receptors, and switching to aripiprazole, which is characterized as a partial D2 receptor agonist, even considering the 20-hour half-life of risperidone and 75-hour half-life of aripiprazole.

**Conclusions**

We report a case of PPA in catatonic schizophrenia that was successfully treated by switching to aripiprazole from risperidone. In our case, the patient’s positive symptoms may have been improved by ECT and risperidone. However, his negative symptoms did not improve because he was suffering from PPA. After we noticed his PPA and changed his treatment to aripiprazole from risperidone, his symptoms and quality of life improved dramatically because his PPA disappeared. One year after discharge, his condition has been maintained. Thus, in this case, PPA may have been a side effect of risperidone. Moreover, aripiprazole, which is characterized by partial agonism of D2 receptors, was very effective. In our case, the patient’s positive symptoms may have been improved by ECT and risperidone. In our case, the patient’s positive symptoms may have been improved by ECT and risperidone. In our case, the patient’s positive symptoms may have been improved by ECT and risperidone. In our case, the patient’s positive symptoms may have been improved by ECT and risperidone. In our case, the patient’s positive symptoms may have been improved by ECT and risperidone.

**Declaration of Interest**

None.

**Acknowledgments**

Part of this work was supported by Grants-in-Aid for Scientific Research on Priority Areas Nos. 13770544 and 50284047 from the Ministry of Education, Science, Sports and Culture of Japan. The authors thank all doctors of the Department of Psychiatry, Shimane University of Medicine for their help with ECT treatment.

**References**

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