

University of Wollongong

Research Online

Faculty of Science, Medicine and Health -
Papers: part A

Faculty of Science, Medicine and Health

2011

Potential control of risperidone-related cognitive deficits by adjunctive aripiprazole treatment

Chang-Hua Hu

University of Wollongong

Nagesh Pai

University of Wollongong, nagesh@uow.edu.au

Xu-Feng Huang

University of Wollongong, xhuang@uow.edu.au

Chao Deng

University of Wollongong, chao@uow.edu.au

Follow this and additional works at: <https://ro.uow.edu.au/smhpapers>



Part of the [Medicine and Health Sciences Commons](#), and the [Social and Behavioral Sciences Commons](#)

Recommended Citation

Hu, Chang-Hua; Pai, Nagesh; Huang, Xu-Feng; and Deng, Chao, "Potential control of risperidone-related cognitive deficits by adjunctive aripiprazole treatment" (2011). *Faculty of Science, Medicine and Health - Papers: part A*. 1391.

<https://ro.uow.edu.au/smhpapers/1391>

Research Online is the open access institutional repository for the University of Wollongong. For further information contact the UOW Library: research-pubs@uow.edu.au

Potential control of risperidone-related cognitive deficits by adjunctive aripiprazole treatment

Abstract

We have read with great interest Uchida and colleagues' paper in your journal (2009; 29: 571–576), which reported that a high dosage of risperidone had a negative impact on cognition in older patients with schizophrenia. This finding is consistent with that of a previous study of a younger patient group showing that schizophrenia patients under high antipsychotic dosage have poor cognitive function performance....

Keywords

CMMB

Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

Publication Details

Hu, C., Pai, N. Brahmavar., Huang, X. & Deng, C. (2011). Potential control of risperidone-related cognitive deficits by adjunctive aripiprazole treatment. *Journal of Clinical Psychopharmacology*, 31 (1), 135-136.

Title: Potential control of risperidone related cognitive deficits by adjunctive aripiprazole treatment

Authors: Chang-Hua Hu, PhD^{1,2}, Nagesh Pai, MD³, Xu-Feng Huang, PhD, MD^{2,4}, Chao Deng, PhD^{2,4,*}

1: School of Pharmaceutical Sciences, Southwest University, Chongqing 400716, China

2: Centre for Translational Neuroscience, School of Health Sciences, University of Wollongong, Wollongong, 2522, NSW, Australia

3: Graduate School of Medicine, University of Wollongong, NSW 2522, Australia

4: Schizophrenia Research Institute, 384 Victoria Street, Darlinghurst, 2010, NSW, Australia

***Corresponding author:**

Dr Chao Deng, School of Health Sciences, University of Wollongong, Wollongong, 2522, NSW, Australia

E-mail: chao@uow.edu.au, Tel: (+61 2) 4221 4934, Fax: (+61 2) 4221 4096

Role of Funding Source

This study was supported by the University of Wollongong and the Schizophrenia Research Institute, Australia, utilising infrastructure funding from NSW Health; these sources had no further role in writing or the decision to submit the paper for publication.

Conflict of Interest:

All authors declare that they have no conflicts of interest.

Key words: Aripiprazole, risperidone, dopamine D2 receptor, cognitive function

Editors,

We have read with great interest Uchida and colleagues' paper in your journal (2009; 29: 571–576), which reported that a high dosage of risperidone had a negative impact on cognition in older patients with schizophrenia¹. This finding is consistent with that of a previous study of a younger patient group showing that schizophrenia patients under high antipsychotic dosage have poor cognitive function performance². One key issue is how to control risperidone related attention deficit. Uchida and colleagues suggested minimizing the adverse effects of risperidone on cognitive function by identifying/using the lowest effective dose of antipsychotics in schizophrenia patients¹. Although very valuable, a low dosage of risperidone may also cause adverse effects on cognitive function³, which could be particularly problematic in aged patients due to age-related pharmacodynamic and pharmacokinetic changes⁴. It is very important that Uchida and colleagues identified that attention deficits induced by risperidone negatively correlated with dopamine D2 receptor blockade¹. We propose that an adjunctive aripiprazole administration with risperidone could be an effective method to control risperidone related attention deficits (and other cognitive deficits) through improving D2 receptor activity.

Aripiprazole is a newly introduced antipsychotic drug that has a favourable safety and tolerability profile⁵, particularly in the elderly patients⁴. Aripiprazole was developed as a potent D2 partial-agonist, 5-HT_{1A} partial-agonist, and also 5-HT_{2A} antagonist⁴, however, recent studies have suggested that aripiprazole is not a simple

partial-agonist, but a functionally selective drug that can act as a D2 agonist or D2 antagonist depending on different brain regions^{6,7}. It is possible that aripiprazole could be used to control risperidone related attention deficits (caused by dopamine D2 receptor blockage) through its D2 agonistic effect. In fact, aripiprazole can preferentially increase dopamine release in the medial prefrontal cortex and hippocampus⁸ and dopamine synthesis in the nucleus accumbens⁶. A recent study has shown that typical antipsychotic treatment resulted in hypoactivation in the dorsal anterior cingulate cortex, which could be improved after switching to aripiprazole and is correlated with improved performance of working memory⁹. Findling *et al.*¹⁰ examined the effectiveness and cognitive effects of aripiprazole in children with a primary diagnosis of attention-deficit/hyperactivity disorder (ADHD), and showed that aripiprazole led to clinical benefit in reducing ADHD symptoms and improving cognition functioning. Moreover, adjunctive aripiprazole treatment has been trialled in risperidone related hyperprolactinemia^{11,12} and olanzapine/clozapine-induced obesity^{13,14}. These studies showed that adjunctive treatment using aripiprazole with other antipsychotics (such as risperidone and olanzapine) was generally safe and well tolerated, and is effective even without reducing the original doses of other antipsychotics^{4,11,13,14}. Therefore, co-administration of aripiprazole and risperidone will result in multiple pharmacological actions and improve the adverse effects beyond the attention deficits (such as weight gain¹⁵). Of course, further animal studies and clinical trials are necessary for testing adjunctive aripiprazole/risperidone

treatment, especially in elderly patients that are at increased risk from drug–drug interactions.

References

1. Uchida H, Rajji T, Mulsant B, Kapur S, Pollock B, Graff-Guerrero A, Menon M, Mamo D. D2 receptor blockade by risperidone correlates with attention deficits in late-life schizophrenia. *Journal of Clinical Psychopharmacology*. 2009;29(6):571-575.
2. Hori H, Noguchi H, Hashimoto R, Nakabayashi T, Omori M, Takahashi S, Tsukue R, Anami K, Hirabayashi N, Harada S, Saitoh O, Iwase M, Kajimoto O, Takeda M, Okabe S, Kunugi H. Antipsychotic medication and cognitive function in schizophrenia. *Schizophrenia Research*. 2006;86(1-3):138-146.
3. Hughes AM, Lynch P, Rhodes J, Ervine CM, Yates RA. Electroencephalographic and psychomotor effects of chlorpromazine and risperidone relative to placebo in normal healthy volunteers. *British Journal of Clinical Pharmacology*. 1999;48(3):323-30.
4. Kohen I, Lester P, Lam S. Antipsychotic treatments for the elderly: efficacy and safety of aripiprazole. *Neuropsychiatric Disease and Treatment*. 2010;6(2):47-58.
5. DeLeon A, Patel NC, Lynn Crismon M. Aripiprazole: A comprehensive review of its pharmacology, clinical efficacy, and tolerability. *Clinical Therapeutics*. 2004;26(5):649-666.
6. Han M, Huang XF, Deng C. Aripiprazole differentially affects mesolimbic and nigrostriatal dopaminergic transmission: implications for long-term drug efficacy and low extrapyramidal side-effects. *International Journal of Neuropsychopharmacology*. 2009;12(7):941-952.
7. Urban JD, Vargas GA, von Zastrow M, Mailman RB. Aripiprazole has functionally selective actions at dopamine D2 receptor-mediated signaling pathways. *Neuropsychopharmacology*. 2007;32(1):67-77.
8. Li Z, Ichikawa J, Dai J, Meltzer HY. Aripiprazole, a novel antipsychotic drug, preferentially increases dopamine release in the prefrontal cortex and hippocampus in rat brain. *European Journal of Pharmacology*. 2004;493(1-3):75-83.
9. Schlagenhauf F, Dinges M, Beck A, Wüstenberg T, Friedel E, Dembler T, Sarkar R, Wrase J, Gallinat J, Juckel G, Heinz A. Switching schizophrenia patients from typical neuroleptics to aripiprazole: Effects on working memory dependent functional activation. *Schizophrenia Research*. 2010;118(1-3):189-200.
10. Findling RL, Short EJ, Leskovec T, Townsend LD, Demeter CA, McNamara NK, Stansbrey RJ. Aripiprazole in children with attention-deficit/hyperactivity disorder. *Journal of Child & Adolescent Psychopharmacology*. 2008;18(4):347-54.
11. Kane J, Correll C, Goff D, Kirkpatrick B, Marder S, Vester-Blokland E, Sun W, Carson W, Pikalov A, Assunção-Talbott S. A multicenter, randomized, double-blind, placebo-controlled, 16-week study of adjunctive aripiprazole for schizophrenia or schizoaffective disorder inadequately treated with quetiapine or risperidone monotherapy. *Journal of clinical psychiatry*. 2009;70(10):1348-1357.
12. Lian J, X-F. H, Pai N, Deng C. Potential control of antipsychotic-induced hyperprolactinemia and obesity in children and adolescents by aripiprazole. *Prog Neuropsychopharmacol Biol Psychiatry*. 2010;2010 Apr 8. [Epub ahead of print.

13. Henderson DC, Fan X, Copeland PM, Sharma B, Borba CP, Boxill R, Freudenreich O, Cather C, Evins AE, Goff DC. Aripiprazole added to overweight and obese olanzapine-treated schizophrenia patients. *Journal of Clinical Psychopharmacology*. 2009;29(2):165-9.
14. Henderson DC, Kunkel L, Nguyen DD, Borba CP, Daley TB, Louie PM, Freudenreich O, Cather C, Evins AE, Goff DC. An exploratory open-label trial of aripiprazole as an adjuvant to clozapine therapy in chronic schizophrenia.[see comment]. *Acta Psychiatrica Scandinavica*. 2006;113(2):142-7.
15. Patel JK, Buckley PF, Woolson S, Hamer RM, McEvoy JP, Perkins DO, Lieberman JA, for the Ci. Metabolic profiles of second-generation antipsychotics in early psychosis: Findings from the CAFE study. *Schizophrenia research*. 2009;111(1-3):9-16.