# Is there protective haplotype of dysbindin gene (DTNBP1) 3 polymorphisms for major depressive disorder

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## Abstract

Dysbindin gene has been repeatedly associated with psychiatric disorders and schizophrenia in particular. This study aimed to investigate the variants of dysbindin gene in major depressive disorder (MDD). One hundred and eighty eight patients with MDD and 350 controls were investigated for 4 variants within the dysbindin gene (rs3213207 A/G, rs1011313 C/T, rs760761 C/T, and rs2619522 A/C). Haplotype analyses revealed a significant association with MDD ($p=0.0007$, protective A-C-T-A and A-C-C-C haplotypes), in particular the effect was due to the rs760761 (C/T) and rs2619522 (A/C) haplotype ($p=0.000026$). These results suggest a protective effect of some dysbindin gene haplotypes on the development of MDD. Coupled with previous findings on schizophrenia, our finding suggests that dysbindin gene variants may have a role in the susceptibility to MDD. Adequately powered further studies in different ethnic groups are warranted.
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*Keywords:* Dysbindin gene; Haplotype; Major depression

## 1. Introduction

Dysbindin (dystrobrevin-binding-protein 1, DTNBP1) is an evolutionary conserved protein similar to that of mouse ortholog (Benson et al., 2001), which is expressed in variable region of human brain (Straub et al., 2002).

Several evidences showed that dysbindin should be involved in synaptic function and modulate neuronal receptors. Dysbindin binds to β-dystrobrevin and is likely to be a component of the dystrophin protein complex (DPC) found in postsynaptic densities (Blake et al., 1999; Roberts, 2001). Interestingly, DPC is involved in the process of signal transduction such as regulating nicotinic receptor cluster and recruiting specific signaling molecules like neuronal nitric oxide synthase (Bredt, 1999; Grady et al., 2000).

Meanwhile, *DTNBP1* [MIM607145] on 6p22.3 has been currently recognized as one of the most eminent susceptibility genes for schizophrenia. The association of *DTNBP1* with schizophrenia has been proven in a number of case–control and family-based association studies in different ethnic populations, as well as it has proven its possible role through gene expression and epigenetic studies for schizophrenia (Bray et al., 2005; DeRosse et al., 2006; Duan et al., 2007; Fanous et al., 2005;

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Table 1
Single marker genotype analysis in case–control samples and clinical features

| | rs3213207 | | | rs1011313 | | | rs760761 | | | rs2619522 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Genotypes | A/A | G/A | G/G | C/C | T/C | T/T | C/C | T/C | T/T | A/A | A/C | C/C |
| **Diagnosis** | | | | | | | | | | | | |
| Case (%) | 180(95.7) | 8(4.3) | 0(0) | 130(69.15) | 53(28.2) | 5(2.7) | 148(78.7) | 37(19.7) | 3(1.6) | 145(77.1) | 40(21.3) | 3(1.6) |
| Controls (%) | 337(96.3) | 13(3.7) | 0(0) | 221(63.1) | 112(32.0) | 17(4.9) | 285(81.4) | 62(17.7) | 3(0.9) | 286(81.7) | 60(17.1) | 4(1.1) |
| | Chi-square=0.09 $df$=1 $p$=0.76 | | | Chi-square=2.81 $df$=2 $p$=0.025 | | | Chi-square=0.94 $df$=2 $p$=0.63 | | | Chi-square=1.61 $df$=2 $p$=0.45 | | |
| Alleles | A | | G | C | | T | C | | T | A | | C |
| Case (%) | 368 | | 8 | 313 | | 63 | 333 | | 43 | 330 | | 46 |
| Controls (%) | 687 | | 26 | 554 | | 146 | 632 | | 68 | 632 | | 68 |
| | $p$=0.2017 | | | $p$=0.1069 | | | $p$=0.4008 | | | $p$=0.2132 | | |
| **Suicide attempt** | | | | | | | | | | | | |
| Yes (%) | 126(96.2) | 5(3.8) | 0(0) | 93(71.0) | 36(27.5) | 2(1.5) | 102(77.9) | 26(19.85) | 3(2.3) | 30(22.9) | 98(74.8) | 3(2.3) |
| No (%) | 11(91.7) | 1(8.3) | 0(0) | 7(58.3) | 5(41.7) | 0(0) | 9(75.0) | 3(25.0) | 0(0) | 2(16.7) | 10(83.3) | 0(0) |
| | Chi-square=0.45 $df$=1 $p$=0.50 | | | Chi-square=1.30 $df$=2 $p$=0.52 | | | Chi-square=0.67 $df$=2 $p$=0.71 | | | Chi-square=0.84 $df$=2 $p$=0.66 | | |
| **Family history** | | | | | | | | | | | | |
| Positive (%) | 103(95.4) | 5(4.6) | 0(0) | 74(68.5) | 32(29.6) | 2(1.85) | 81(75.0) | 25(23.15) | 2(1.85) | 26(24.1) | 80(74.1) | 2(1.85) |
| Negative(%) | 34(97.1) | 1(2.9) | 0(0) | 26(74.3) | 9(25.7) | 0(0) | 30(85.7) | 4(11.4) | 1(2.9) | 6(17.1) | 28(80.0) | 1(2.9) |
| | Chi-square=0.22 $df$=1 $p$=0.64 | | | Chi-square=1.39 $df$=2 $p$=0.50 | | | Chi-square=2.53 $df$=2 $p$=0.28 | | | Chi-square=0.84 $df$=2 $p$=0.66 | | |
| **Age at onset** | | | | | | | | | | | | |
| Mean (SD) | 41.7($\pm$15.4) | 33.8($\pm$13.8) | – | 39.8($\pm$16.1) | 45.7($\pm$12.8) | 29.5($\pm$6.4) | 41.8($\pm$14.9) | 40.2($\pm$17.0) | 38.7($\pm$23.2) | 41.1($\pm$15.7) | 41.6($\pm$15.2) | 38.7($\pm$23.2) |
| | $F$=1.52 $df$=1140 $p$=0.22 | | | $F$=2.82 $df$=2139 $p$=0.06 | | | $F$=0.16 $df$=2139 $p$=0.85 | | | $F$=0.06 $df$=2139 $p$=0.94 | | |
| **Number of admission** | | | | | | | | | | | | |
| Mean (SD) | 1.4($\pm$1.0) | 1.2($\pm$0.4) | – | 1.4($\pm$0.9) | 1.5($\pm$1.0) | 1.5($\pm$0.7) | 1.5($\pm$1.0) | 1.3($\pm$0.8) | 1.0($\pm$0.1) | 1.3($\pm$0.8) | 1.5($\pm$1.0) | 1.0($\pm$0.1) |
| | $F$=0.50 $df$=1140 $p$=0.48 | | | $F$=0.09 $df$=2139 $p$=0.91 | | | $F$=0.70 $df$=2139 $p$=0.50 | | | $F$=0.73 $df$=2139 $p$=0.48 | | |