BDNF Gene Polymorphisms and Chronic Postsurgical Pain

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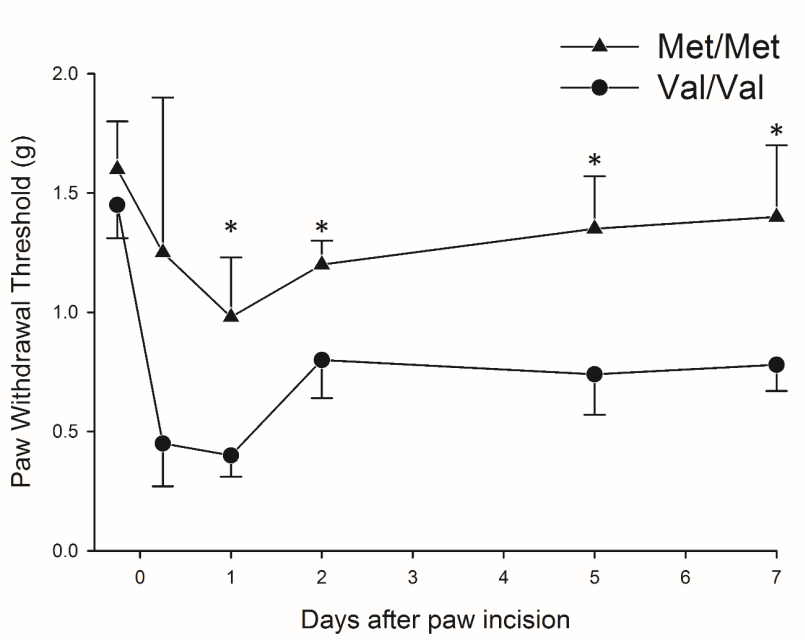
Background: Chronic postsurgical pain affects at least 10% of patients undergoing common operations and adversely affects their quality of life. We evaluated the genetic association between single-nucleotide polymorphisms (SNPs) and chronic postsurgical pain.

Methods: Using GoldenGate genotyping assays, we genotyped 768 SNPs within 65 pain-related genes in 1,152 surgical patients who were enrolled in our Persistent Pain After Surgery Study. Patients were contacted by phone to determine if they had chronic postsurgical pain at 12 months. SNPs identified were validated in a matched cohort of 103 patients with chronic postsurgical pain and another 103 patients who were pain-free. Functional role of the targeted SNP was tested in an experimental plantar incision pain model using knock-in mice.

Results: At 12 months after surgery, 246 (21.4%) patients reported chronic postsurgical pain. SNPs located in brain-derived neurotrophic factor (*BDNF*) gene (*rs6265* and *rs1491850*) were significantly associated with chronic postsurgical pain, p=0.003 and 0.004, respectively. The effects of both SNPs were confirmed in the validation cohort, p=0.005 and 0.002, respectively. Age <65 years, male gender, low education level and prior history of pain syndrome were found to increase risk of chronic postsurgical pain. The two SNPs had higher population attributable risk (6.25-12.3%) compared with clinical risk factors (3.71-8.76%). Importantly, the functional role of *rs6265*, which is a non-synonymous SNP, was confirmed with less mechanical allodynia in $BDNF^{Met/Met}$ mice compared with $BDNF^{Val/Val}$ group after plantar incision (Figure 1).
Conclusions: This study demonstrated that genetic variations of *BDNF* is important in determining the susceptibility to chronic postsurgical pain.

Figure 1. Incisional pain mouse model. A 10-mm longitudinal incision was made on the plantar surface of the left hind paw. Changes in paw withdrawal in response to pressure using von Frey filaments in $BDNF^{Met}$ knock-in (Met/Met) and wild-type (Val/Val) mice (n = 15 per group). *, $p < 0.05$, repeated measures analysis of variance; Values are mean ± standard error.


Met/Met
Val/Val
Paw Withdrawal Threshold (g)
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
Days after paw incision
*
*
*
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