



Behavioral effects of Bcl-2 deficiency: implications for affective disorders

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Abstract:

New hypotheses regarding affective disorders suggest a critical role for cellular resilience and plasticity. Bcl-2 is a central protein in these processes and is elevated by mood stabilizers and antidepressants. In previous studies, mice with targeted mutations of Bcl-2 showed anxiety-related behavioral changes. The present study further explored the relationship between Bcl-2 and behavior using mice with a targeted mutation but with a different background strain than previously tested.

Bcl-2 heterozygous mice (B6;129S2-Bcl-2^{tm1Sjk>/J}) were tested in models of depression, mania and anxiety. Compared to Wild Type (WT) controls, mutant mice showed behaviors modeling two facets of mania: increased reward seeking and amphetamine sensitization. Moreover, the sensitization was attenuated by chronic pretreatment with lithium. In contrast to previous data, the mutation did not affect measures of anxiety. Although data are still minimal, it supports additional studies of the role of Bcl-2 in affective and anxiety disorders. The importance of background strain in behavioral phenotypes of mutant mice is known and the current lack of effect on anxiety measures may be related to high baseline anxiety of WT animals. More precise studies of Bcl-2 in affective and anxiety disorders will be possible when specific pharmacological modulators of Bcl-2 become available.

Key words:

animal models, bipolar disorder, mania, depression, Bcl proteins
