Science of the Total Environment xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Weight of evidence evaluation of a network of adverse outcome pathways linking activation of the nicotinic acetylcholine receptor in honey bees to colony death

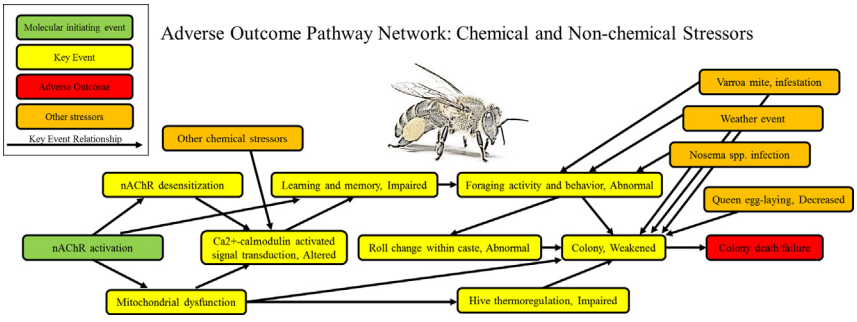
Carlie A. LaLone [a,*], Daniel L. Villeneuve [a], Judy Wu-Smart [b], Rebecca Y. Milsk [c], Keith Sappington [d], Kristina V. Garber [d], Justin Housenger [d], Gerald T. Ankley [a]

[a] U.S. Environmental Protection Agency, Office of Research and Development, National Health and Environmental Effects Research Laboratory, Mid-Continent Ecology Division, 6201 Congdon Blvd., Duluth, MN 55804, USA
[b] University of Nebraska-Lincoln, Department of Entomology, 105A Entomology Hall, Lincoln, NE 68583, USA
[c] ORISE Research Participation Program, U.S. Environmental Protection Agency, Office of Research and Development, National Health and Environmental Effects Research Laboratory, Mid-Continent Ecology Division, 6201 Congdon Blvd., Duluth, MN 55804, USA
[d] U.S. Environmental Protection Agency, Office of Pesticide Programs, Washington D.C. 20460, USA

HIGHLIGHTS

- Six AOPs were developed describing perturbation of the honey bee nicotinic acetylcholine receptor leading to colony death.
- From weight of evidence evaluation, sufficient biological plausibility exists to link activation of nAChR to colony death.
- Uncertainties remain in the AOP descriptions, identifying knowledge gaps that can guide future research.
- These AOPs provide a foundation for future collaborations to understand chemical and non-chemical stressors on bee colonies.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 18 November 2016
Received in revised form 17 January 2017
Accepted 18 January 2017
Available online xxxx

Editor: Jay Gan

Keywords:
Adverse outcome pathway
Honey bee
Nicotinic acetylcholine receptor activation
Colony loss
Neonicotinoids
Network

ABSTRACT

Ongoing honey bee (*Apis mellifera*) colony losses are of significant international concern because of the essential role these insects play in pollinating crops. Both chemical and non-chemical stressors have been implicated as possible contributors to colony failure; however, the potential role(s) of commonly-used neonicotinoid insecticides has emerged as particularly concerning. Neonicotinoids act on the nicotinic acetylcholine receptors (nAChRs) in the central nervous system to eliminate pest insects. However, mounting evidence indicates that neonicotinoids also may adversely affect beneficial pollinators, such as the honey bee, via impairments on learning and memory, and ultimately foraging success. The specific mechanisms linking activation of the nAChR to adverse effects on learning and memory are uncertain. Additionally, clear connections between observed impacts on individual bees and colony level effects are lacking. The objective of this review was to develop adverse outcome pathways (AOPs) as a means to evaluate the biological plausibility and empirical evidence supporting (or refuting) the linkage between activation of the physiological target site, the nAChR, and colony level consequences. Potential for exposure was not a consideration in AOP development and therefore this effort should not be considered a risk assessment. Nonetheless, development of the AOPs described herein has led to the

* Corresponding author at: 6201 Congdon Blvd., Duluth, MN 55804, USA.
E-mail address: LaLone.Carlie@epa.gov (C.A. LaLone).

http://dx.doi.org/10.1016/j.scitotenv.2017.01.113
0048-9697/Published by Elsevier B.V.

identification of research gaps which, for example, may be of high priority in understanding how perturbation of pathways involved in neurotransmission can adversely affect normal colony functions, causing colony instability and subsequent bee population failure. A putative AOP network was developed, laying the foundation for further insights as to the role of combined chemical and non-chemical stressors in impacting bee populations. Insights gained from the AOP network assembly, which more realistically represents multi-stressor impacts on honey bee colonies, are promising toward understanding common sensitive nodes in key biological pathways and identifying where mitigation strategies may be focused to reduce colony losses.

Published by Elsevier B.V.

Contents

Please cite this article as: LaLone, C.A., et al., Weight of evidence evaluation of a network of adverse outcome pathways linking activation of the nicotinic acetylcholine receptor ..., Sci Total Environ (2017), http://dx.doi.org/10.1016/j.scitotenv.2017.01.113