- 1 Letter to the Editor
- 2 (discussing Volkow ND, Swanson JM, Evins E, et al. Effects of cannabis use
- 3 on human behavior, including cognition, motivation, and psychosis: A review.
- 4 *JAMA Psychiatry.* 2016;73(3):292-297.)

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- 7 Title: The effects of cannabis use on human behavior: a call for
- standardization of cannabis use metrics 8

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- 19 Conflict of Interest Disclosures: None reported.

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21 Word count: 399

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24 standardization of cannabis use metrics 25 26 To the Editor With rapidly shifting legislation worldwide in relation to recreational and medicinal cannabis use, the review by Volkow et al¹ is timely. 27 28 We highlight several additional noteworthy issues for consideration. 29 While further evidence has emerged that acute and chronic exposure to cannabis impairs cognition,² there is still grossly insufficient evidence for 30 31 recovery of function with abstinence. Neither the parameters of cannabis 32 exposure nor the neural mechanisms subserving persistence or recovery 33 have been elucidated. Well-controlled prospective studies monitoring 34 restoration of brain function and structure from current use through prolonged 35 abstinence are required to delineate the time course and moderators of 36 potential recovery of cognitive function. Volkow et al¹ cite evidence that cannabidiol may protect against some harmful 37 38 cognitive effects. We have evidence that cannabidiol may also protect against structural brain harms^{3,4} (eg, hippocampal neural integrity and volume loss in 39 cannabis users⁴) which are also restored with prolonged abstinence.⁴ This 40 41 potential neuroprotective property of cannabidiol is promising for 42 implementation in harm minimization and therapeutic strategies for a range of 43 conditions, including cannabis dependence. 44 Vokow et al¹ guery the generalization of chronic effects on cognition and 45 motivation claiming that many study samples include a large proportion of 46 cannabis dependent individuals. We find that formal diagnostic assessment of

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47	cannabis use disorders is rarely performed in neurocognitive studies ⁵ and
48	cognitive deficits in recreational users are associated with varying cannabis
49	use parameters. ² We suggest further investigation of specific neural
50	alterations that dissociate dependence from non-problem use, toward the
51	development of neurobiological models of cannabis addiction and related
52	harms. ^{3,5}
53	Acute intoxication broadly impairs multiple aspects of cognition that are likely
54	to affect users in daily life. An assumption that frequent cannabis users
55	develop tolerance to its adverse cognitive effects has little empirical
56	evidence. ² While cognitive impairments may be blunted in regular users
57	following acute intoxication, they are nevertheless evident across multiple
58	domains (psychomotor, attention, memory), with potential real-world effects
59	on complex tasks such as driving.
60	We agree with Volkow et al ¹ that "there is a need to clarify which aspects of
61	cannabis exposure (eg, age at initiation, quantity used, frequency of use,
62	duration of use, and potency of cannabis used) confer the greatest risk for
63	adverse consequences". Further, we advocate for greater standardization of
64	cannabis use metrics by consensus to quantify various parameters of
65	cannabis exposure in humans, 2,3,5 which will serve as a starting point for
66	addressing the many outstanding questions regarding its effects on human
67	behavior.

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- 1. Volkow ND, Swanson JM, Evins E, et al. Effects of cannabis use on
- human behavior, including cognition, motivation, and psychosis: A review.
- 75 *JAMA Psychiatry*. 2016;73(3):292-297.
- 76 2. Broyd SJ, van Hell HH, Beale C, Yücel M, Solowij N. Acute and chronic
- 77 effects of cannabinoids on cognition a systematic review. *Biol*
- 78 *Psychiatry*. 2016;79(7):557–567.
- 79 3. Lorenzetti V, Solowij N, Yücel M. The role of cannabinoids in
- 80 neuroanatomic alterations in cannabis users. *Biol Psychiatry*.
- 81 2016;79(7):e17-e31.
- 4. Yücel M, Lorenzetti V, Suo C, et al. Hippocampal harms, protection and
- recovery following regular cannabis use. *Transl Psychiatry*. 2016;6:e710.
- 84 5. Lorenzetti V, Cousijn J, Solowij N, et al. Cannabis use disorders: A call for
- evidence. Front Behav Neurosci. 2016;10:86.

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