Psychopharmacology
https://doi.org/10.1007/s00213-019-05242-y

LETTER TO EDITOR

Acquired synaesthesia following 2C-B use

Steliana Yanakieva[1] · David P. Luke[2] · Ashok Jansari[1] · Devin B. Terhune[1]

Received: 9 January 2019 / Accepted: 27 March 2019

Psychedelic drugs reliably trigger experiences that closely resemble *synaesthesia* (Luke and Terhune 2013), a condition in which inducer stimuli will reliably and automatically elicit atypical concurrent experiences (Ward 2013). These transient episodes are considered controversial because they do not meet behavioural diagnostic criteria for developmental synaesthesia (Terhune et al. 2016). However, if these behavioural markers are attributable to the consolidation of synaesthetic associations over time (Terhune et al. 2016), they should be observed in cases of acquired synaesthesia. Here we report a case of drug-induced acquired synaesthesia (LW) that meets standard diagnostic criteria for developmental synaesthesia.

LW is a 29-year-old male who reports continuously experiencing multiple forms of synaesthesia for over 7 years since ingesting approximately 70–150 mg of 2,5-dimethoxy-4-bromophenethylamine (2C-B) (Papaseit et al. 2018), which greatly exceeds the normal dosage (12–24 mg) (Shulgin and Shulgin 1990) (see Supplementary Materials). LW was contrasted against 10 non-synaesthete healthy controls, all of whom provided informed written consent. He reports that his synaesthetic associations became more stable over time and his response patterns met inducer-concurrent consistency thresholds for week-colour and instrument-colour, but not chord-colour, synaesthesia on a standardized battery (Eagleman et al. 2007). He experiences colours as visuospatially co-localized with inducing faces (projector synaesthesia (Dixon et al. 2004; Terhune et al. 2015)), which was corroborated (Skelton et al. 2009). He reports that none of his immediate family members have developmental synaesthesia; two individuals who have known him since before the onset of his synaesthesia independently corroborated his reports. The transient induction of synaesthesia-like experiences through 2C-B use has been widely reported in online discussion forums of recreational drug users as well as in a previous survey of drug users (Luke et al. 2012), but we are unaware of any reports of acquired synaesthesia through the use of 2C-B or any other drugs.

To assess the automaticity of LW's face-colour synaesthesia, one of the hallmark behavioural features of developmental synaesthesia (Ward 2013), he was contrasted against controls on a priming task in which face primes were presented prior to judgments of colour patches that were either congruent or incongruent with the preceding prime according to LW's face-colour associations. LW displayed a larger congruency effect (incongruent–congruent) in error rates, 80% [95% CIs 71, 88], than controls, 2% [0.2, 2.6], $t(9) = 37.13$, $p < .001$ (Fig. 1), reflecting a difference of nearly 39 SDs, $z_{cc} = 38.95$ [38.40, 39.56], with a very low probability of occurrence in the general population, $p_{gp} = 1.8^{-9}\%$ [1.6^{-9}, 2.1^{-9}]. LW's congruency effect in response times for correct responses was also larger, 236 ms [24, 507], than that of controls, 20 ms [− 1, 48], $t(9) = 5.07$, $p < .001$, corresponding to a difference of over 5 SDs, $z_{cc} = 5.32$ [4.63, 5.83], and a very low probability of occurrence, $p_{gp} = 3^{-2}\%$ [2^{-2}, 8^{-2}]. Bootstrap resampling revealed that LW's response distributions in congruent and incongruent conditions were completely independent for error rates and only minimally overlapping for response times whereas both sets of distributions overlapped considerably in controls.

LW's multiple forms of synesthesia exhibited inducer-concurrent consistency and his face-colour synesthesia exhibited automaticity, thereby meeting the two most widely used behavioural diagnostic criteria for synesthesia (Eagleman et al. 2007; Rothen et al. 2013; Ward 2013). Insofar as these criteria are not met by transient episodes of drug-induced synaesthesia, these results are consistent

This study was previously presented at *Bridging senses: New developments in synesthesia* (Royal Society, London, UK, 22–23 October 2018).

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00213-019-05242-y) contains supplementary material, which is available to authorized users.

✉ Devin B. Terhune
d.terhune@gold.ac.uk

[1] Department of Psychology, Goldsmiths, University of London, New Cross, London SE14 6NW, UK

[2] Department of Psychology, Social Work and Counselling, University of Greenwich, London, UK

Published online: 26 April 2019

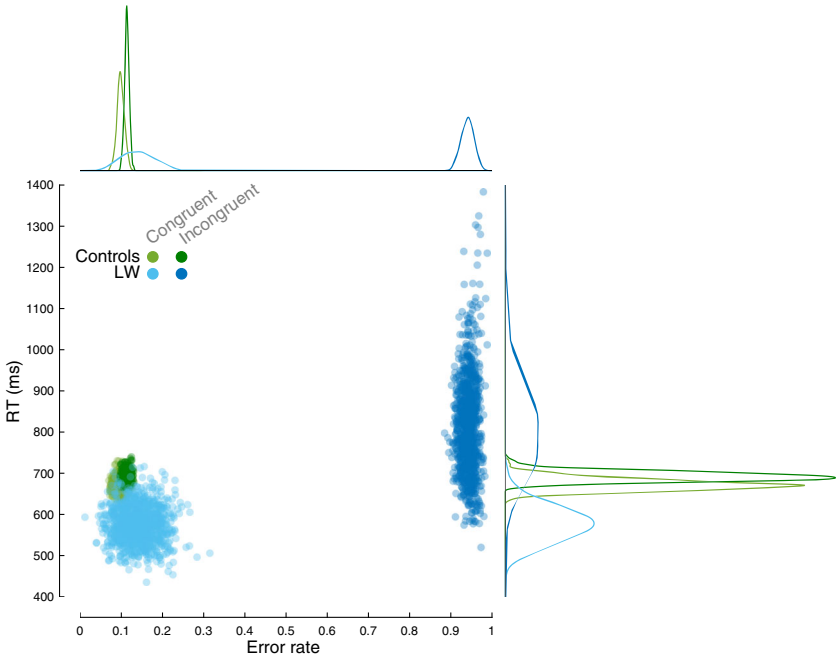

Fig. 1 Face-colour automaticity in an acquired synaesthete (LW) and controls. Markers reflect 1000 bootstrap resamples for LW and control means in congruent and incongruent face-colour priming conditions. Marginal histograms reflect kernel density plots of the bootstrap distributions

with the proposal that automaticity and consistency are byproducts of the over-learning of associations rather than behavioural signatures of synaesthesia per se (Terhune et al. 2016).

Insofar as 2C-B is a partial serotonin agonist (Páleníček et al. 2013; Papaseit et al. 2018), these results add to a growing body of evidence implicating serotonin in the development of synaesthesia (Brogaard and Gatzia 2016; Luke and Terhune 2013). Although LW did not experience synaesthesia prior to consuming 2C-B, we cannot rule out the possibility that 2C-B use interacted with a latent predisposition for cortical disinhibition or hyperexcitability (Rothen and Meier 2014; Terhune et al. 2015). The factors that sustained his synaesthesia are unknown, but its continuity is plausibly attributable to the excessive dose of 2C-B (Shulgin and Shulgin 1990). Excessive serotonin from LW's 2C-B use (Papaseit et al. 2018) may have triggered elevated glutamate release, and concomitant hyperexcitability in visual cortex (Brogaard and Gatzia 2016), a neurophysiological characteristic of synaesthesia (Terhune et al. 2015; Terhune et al. 2011). Cortical hyperexcitability may have triggered sustained visual colour percepts that were perceived as visuospatially co-localized with environmental inducers similar to the induction of hallucinogen persisting perception disorder (HPPD), which may also have a serotonergic basis (Litjens et al. 2014; Martinotti et al. 2018).

Authors' contribution SY: study concept and design, data acquisition, analysis and interpretation of data, and drafting/revising the manuscript. DPL: study concept and design, data interpretation, and revising the manuscript. AJ: study concept and design, data interpretation, and revising the manuscript. DBT: study concept and design, data acquisition, analysis and interpretation of data, and drafting/revising the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interests.

References

Brogaard B, Gatzia DE (2016) Psilocybin, LSD, mescaline and drug-induced synesthesia. In: Preedy VR (ed) Neuropathology of drug addictions and substance misuse. Academic Press, Elsevier, Amsterdam, NL, pp 890–905

Dixon MJ, Smilek D, Merikle PM (2004) Not all synaesthetes are created equal: projector versus associator synaesthetes. Cogn Affect Behav Neurosci 4:335–343

Eagleman DM, Kagan AD, Nelson SS, Sagaram D, Sarma AK (2007) A standardized test battery for the study of synesthesia. J Neurosci Methods 159:139–145

Litjens RP, Brunt TM, Alderliefste GJ, Westerink RH (2014) Hallucinogen persisting perception disorder and the serotonergic system: a comprehensive review including new MDMA-related clinical cases. Eur Neuropsychopharmacol 24:1309–1323

Luke DP, Terhune DB (2013) The induction of synaesthesia with chemical agents: a systematic review. Front Psychol 4:753

Luke D, Terhune D, Friday R (2012) Psychedelic synaesthesia: evidence for a serotonergic role in synaesthesia. Seeing Perceiving 25:74

Martinotti G, Santacroce R, Pettorruso M, Montemitro C, Spano MC, Lorusso M, di Giannantonio M, Lerner AG (2018) Hallucinogen persisting perception disorder: etiology, clinical features, and therapeutic perspectives. Brain Sci 8

Páleníček T, Fujáková M, Brunovský M, Horáček J, Gorman I, Balíková M, Rambousek L, Syslová K, Kačer P, Zach P, Bubeníková-Valešová V, Tylš F, Kubešová A, Puskarčíková J, Höschl C (2013) Behavioral, neurochemical and pharmaco-EEG profiles of the psychedelic drug 4-bromo-2,5-dimethoxyphenethylamine (2C-B) in rats. Psychopharmacology 225:75–93

Papaseit E, Farre M, Perez-Mana C, Torrens M, Ventura M, Pujadas M, de la Torre R, Gonzalez D (2018) Acute pharmacological effects of 2C-B in humans: an observational study. Front Pharmacol 9:206

Rothen N, Meier B (2014) Acquiring synaesthesia: insights from training studies. Front Hum Neurosci 8:109

Rothen N, Seth AK, Witzel C, Ward J (2013) Diagnosing synaesthesia with online colour pickers: maximising sensitivity and specificity. J Neurosci Methods 215:156–160

Shulgin A, Shulgin A (1990) PIHKAL: a chemical love story. Transform Press, Berkeley, CA

Skelton R, Ludwig C, Mohr C (2009) A novel, illustrated questionnaire to distinguish projector and associator synaesthetes. Cortex 45:721–729

Terhune DB, Tai S, Cowey A, Popescu T, Cohen Kadosh R (2011) Enhanced cortical excitability in grapheme-color synesthesia and its modulation. Curr Biol 21:2006–2009

Terhune DB, Murray E, Near J, Stagg CJ, Cowey A, Cohen Kadosh R (2015) Phosphene perception relates to visual cortex glutamate levels and covaries with atypical visuospatial awareness. Cereb Cortex 25:4341–4350

Terhune DB, Luke DP, Kaelen M, Bolstridge M, Feilding A, Nutt D, Carhart-Harris R, Ward J (2016) A placebo-controlled investigation of synaesthesia-like experiences under LSD. Neuropsychologia 88: 28–34

Ward J (2013) Synesthesia. Annu Rev Psychol 64:49–75