Addendum 2019 to
Delius, J. D., & Acerbo, M. J. (2015),
The effects of apomorphine in pigeons: Some supplementary notes
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First we need to rectify a typographic error in the Supplementary notes in the 'Conditioning model supplementation' section: The recurring expression 'apo X cage' should read '**apo x cage**' (meaning: apo state multiplied by cage environment). We must further correct two omissions in the Keller and Delius (2001) paper cited therein. In its 'Results' section, the text should read '… or had not pecked at all (apomorphine-unresponsive birds) were necessarily **excluded from the evaluation.**' The caption under Figure 1 should be: '… percent of total number of pecks directed at apomorphine conditioned **stimuli** …'

We further feel urged to comment on a related paper. Within a study that primarily looked for a dopaminergic effect on their food-reinforced key-pecking in a Skinner box, Anselme, Edes, Tabrik, and Güntürkün (2018) collaterally report on the sensitization shown by 9 pigeons upon repeated daily injections of 0.75 mg/1ml/kg i.m. apomorphine (apo). They employed ingenious 'carbon-box' environments, consisting of cardboard box cages whose inner walls and floor were lined with a white paper, carbon paper, and dotted paper 'sandwich' that was sensitive to the pigeon's apo-pecking. The peck marks left on the innermost white papers during the 30 min exposures to the boxes were digitized and then computer counted. The mean peck counts rose from about 200 / 30 min during session day 1 to around 2.000 / 30 min during session day 8, revealing a quite average sensitization to apo.

When placed in the same cardboard-carbon boxes after being saline injected one month later, the same pigeons emitted only about 100 pecks / 30 min. The pronounced drop in response is in full agreement with equivalent findings reported by us earlier (Acerbo & Delius, 2004; Delius, Acerbo, Krug, Lee, & Leydel, 2015; Keller, Delius, & Acerbo, 2002), especially if some forgetting during the present comparatively long interval between the apomorphine treatment and the saline testing is taken into account. In the somewhat haphazard discussion of their sensitization results, Anselme et al. (2018) however regard this result as negating (see the paper's title!) the Pavlovian conditioned nature of the context-dependent apomorphine sensitization that was supported in our above papers. In doing so, however, they crucially overlooked that the compound quality of the experimental-cage CS under apo influence differs from the straight nature of the same-cage CS under saline 'influence.' This is due to the circumstance that i.m. apomorphine not only elicits pecking, but also strongly affects the dopaminergic retinal functioning of the subjects (Jackson et al., 2012; Kram, Mantey & Corbo, 2010), and perhaps also their tectal functioning (Dietl & Palacios, 1988). This entails that the pigeons' visual percept of the identical environmental context under plain saline must be assumed to be only partially equivalent to what they experienced under the drug apo. Due to the response decrement connected to the attending stimulus generalization, it thus cannot be expected to elicit a similarly intense pecking CR! Relating to the apomorphine conditioned sensitization issue, we also draw attention to the concordant recent findings by Garone Santos, Carey, and Pinheiro Carrera (2018) on the locomotor activity of rats.

The milder drop in response to about 800 pecks / 30 min that Anselme et al. (2018) observed when retesting the same pigeons another month later with a 0.75 mg/1ml/kg i.m. apo dose lies within the sensitization waning with time (=forgetting) reported by Keller et al. (2002), but some of the drop may also be attributable to an aging (=softening) of the cardboard-carbon arrangement employed. Regarding the effects of the apo treatments upon food conditioned key pecking of their pigeons, we are slightly surprised that the authors did not discuss the relevant publication by Pinkston and Lamb (2012) nor referred to other relevant papers quoted therein. We are grateful to Dr. P. Anselm, Bochum, for his willingness to discuss these points with us.

We also draw attention to the publication by Demontis, Serra, and Serra (2017) presenting evidence that the responses elicited by apomorphine in humans are mania related. The apomorphine-induced pecking fits of pigeons may thus also be of manic nature caused by a dopaminergic over-stimulation that is potentiated by the progressive sensitization to the drug. Additionally we want to suggest that a regime of intravenous or intracerebral self-administration such as that proposed by Huskinson, Naylor, Rowlett, and Freeman (2014) might possibly lead to an apomorphine dependency in pigeons.

Another issue that merits an updating comment is the pigeons' behavioral reactivity to near-infrared light noted in connection with the touch-screen apomorphine-pecking experiment that we reported in the Supplementary notes (and also in connection with two other, apomorphine unrelated publications: Delius & Delius, 2019; Delius, Delius, & Lee, 2017). In the meantime, it has become clear that far-infrared light (1000 nm), hitherto thought to be invisible to humans, is in fact quite visible to them due to a shorter wavelength fluorescing of the photo-pigment rhodopsin in retinal rods (Palczewska et al., 2014). Inasmuch as avian rods also incorporate rhodopsin, it is almost certain that birds also perceive far-infrared light in an analogous manner. But this sensitivity is unlikely to extend to the near-infrared 800–950 nm range that was of interest in the above addressed contexts. Remarkably however, both keratin and melanin, the key constituents of pigeons' beaks (as well as their feathers, claws, and irises), which are always within their frontal field of view, are known to exhibit some ultraviolet-far-blue (300–450 nm) fluorescence upon near-infrared (700–900 nm) illumination (Huang et al., 2006; Shcherbakova et al., 2016). This beak (and iris?) fluorescence might mediate the near-infrared reactivity of pigeons observed by us (see also Pinkston, Madden, & Fowler, 2008) as pigeons are known to perceive near-ultraviolet light (Emmerton, 1983; Rubene et al., 2010).

References

Acerbo, M. J., & Delius, J.D. (2004). Behavioral sensitization to apomorphine in pigeons (*Columba livia*): blockade by the D1 dopamine antagonist SCH-23390. *Behavioral Neuroscience, 118,* 1080–1088. https://doi.org/10.1037/0735-7044.118.5.1080

Anselme, P., Edes, N., Tabrik S., & Güntürkün, O. (2018). Long-term behavioral sensitization to apomorphine is independent of conditioning and increases conditioned pecking, but not preference, in pigeons. *Behavioural Brain Research, 336,* 122–134. https://doi.org/10.1016/j.bbr.2017.08.037

Delius, J. D., Acerbo, M., Krug, I., Lee, J., & Leydel, R. (2015). Sensitization to apomorphine in pigeons: The product of a multifactor conditioning process. *Behavioral Pharmacology, 26,* 139–158. https://doi.org/10.1097/FBP.0000000000000087

Delius, J. D, & Delius, J. A. M. (2019). *Pigeons' pixel pattern perception*. Ms. in preparation.

Delius, J. D., Delius, J. A. M., & Lee, J. M. (2017). Generalized symmetry recognition in pigeons or not? *PLoS ONE, 12:* 11. https://doi.org/10.1371/journal.pone.0187541

Demontis, F., Serra, F., & Serra, G. (2017). Antidepressant-induced dopamine receptor dysregulation: A valid animal model of manic-depressive illness. *Current Neuropharmacology, 15*, 417–423. https://doi.org/10.2174/1570159X14666160715165648

Dietl, M. M., & Palacios, J. M. (1988). Neurotransmitter receptors in the avian brain. I. Dopamine receptors. *Brain Research, 439,* 354–359. https://doi.org/10.1016/0006-8993(88)91494-1

Emmerton, J. (1983). Pattern discrimination in the near-ultraviolet by pigeons. *Perception & Psychophysics, 34*, 555–559. https://doi.org/10.3758/bf03205910

Garone Santos, B., Carey, R. J., & Pinheiro Carrera, M. (2018). Repeated pre-trial and post-trial low and high dose apomorphine treatments induce comparable inhibitory/excitatory sensitization and conditioned drug effects. *Pharmacology Biochemistry and Behavior, 175,* 108–115. https://doi.org/10.1016/j.pbb.2018.09.011

Huang, Z., Zeng, H., Hamzavi, I., Alajlan, A., Tan, E., McLean, D. I., & Lui, H. (2006). Cutaneous melanin exhibiting fluorescence emission under near-infrared light excitation. *Journal of Biomedical Optics, 11:* 034010. https://doi.org/10.1117/1.2204007

Huskinson, S. L., Naylor, J. E., Rowlett, J. K., & Freeman, K. B. (2014). Predicting abuse potential of stimulants and other dopaminergic drugs: Overview and recommendations. *Neuropharmacology, 87,* 66–80. https://doi: 10.1016/j.neuropharm.2014.03.009

Jackson, C, R. Ruan, G.-X., Aseem, F., Abey, J., Gamble, K, Stanwood, G., Palmiter, R. D., Iuvone, M., & McMahon, D. G. (2012). Retinal dopamine mediates multiple dimensions of light-adapted vision. *Journal of Neuroscience, 32*, 9359–9368. https://doi.org/10.1523/jneurosci.0711-12.2012

Keller, S., & Delius, J. D. (2001). Discriminative learning occasioned by the administration of a dopamine agonist. *Psychopharmacology, 157,* 320–323. https://doi.org/10.1007/s002130100847

Keller, S., Delius, J. D., & Acerbo, M. (2002). Apomorphine sensitization: Evoking conditions, context dependence, effect persistence and conditioned nature. *Behavioural Pharmacology, 13,* 189–201. https://doi.org/10.1097/00008877-200205000-00002

Kram, Y.A., Mantey, S., & Corbo, J. C. (2010). Avian cone photoreceptors tile the retina as five independent, self-organizing mosaics. *PLoS ONE, 5*: e8992. https://doi.org/10.1371/journal.pone.0008992

Lapierre-Landry, M., Carroll, J., & Skala, M. C. (2018). Imaging retinal melanin: A review of current technologies. *Journal of Biological Engineering, 12:* 29. https://doi.org/10.1186/s13036-018-0124-5

Palczewska, G., Vinberg, F., Stremplewski, P., Bircher, M. P., Salom, D., Komar, K., Zhang, J., Cascella, M., Wojtkowski, M., Kefalov, V. J., & Palczewski, K. (2014). Human infrared vision is triggered by two-photon chromophore isomerization. *Proceedings of the National*

Academy of Sciences of the United States of America, 111(50), E5445–E5454. https://doi.org/10.1073/pnas.1410162111

Pinkston, J. W., & Lamb, R. J. (2012). Reinforcer magnitude attenuates apomorphine's effects on operant pecking. *Journal of the Experimental Analysis of* Behavior, 98, 273–282. https://doi.org/10.1901/jeab.2012.98-273

Pinkston, J. W., Madden G. J., & Fowler, S. C. (2008). Effects of white and infrared lighting on apomorphine–induced pecking in pigeons. *Behavioural Pharmacology, 19,* 347–352. https://doi.org/10.1097/FBP.0b013e32830990acJ

Rubene, D., Håstad, O., Tauson, R., Wall, H., & Ödeen A. (2010). The presence of UV wavelengths improves the temporal resolution of the avian visual system. *Journal of Experimental Biology*, *213*, 3357–3363. https://doi.org/10.122/jeb.04242

Shcherbakova, D. M., Baloban, M., Emelyanov, A. V., Brenowitz, M., Guo, P., & Verkhusha, V. V. (2016). Bright monomeric near-infrared fluorescent proteins as tags and biosensors for multiscale imaging. *Nature Communications*, *7:* 12405. https://doi.org/10.1038/ncomms12405