Final Publishable Report for Post-Ingest Mesolimb (#631404)

Title: Post-ingestive effects on mesolimbic circuitry

Call: FP7-PEOPLE-2013-CIG

This is the final report for the above referenced project, which has supported Dr. James McCutcheon's integration into the European scientific environment. The overarching objective of FP7 Career Integration Grants was to encourage researchers to establish themselves in Europe including supporting researchers in the first steps of their European research career and integrating them into the European scientific community. An emphasis is put on allowing transfer of knowledge that has been acquired prior to the grant onset and developing lasting co-operation with the scientific environment. Accordingly, this document will outline (1) evidence of Dr. McCutcheon's lasting professional integration in Europe and (2) the progress made towards to scientific goals of his project.

Evidence of professional integration

As part of this project, Dr. McCutcheon returned to Europe from >6 years postdoctoral research in the US. In the US, he had become expert at *in vivo* techniques (e.g. voltammetry) and behavioural studies of food and drug intake. Dr McCutcheon was appointed a Lecturer at University of Leicester (UK) and in August 2018 was promoted to Associate Professor. While at Leicester he has contributed immensely to community both within the institution as well as further afield in ways that have enhanced his integration and the transfer of knowledge from US to Europe.

(1) He organized the department's seminar program from 2015-2018, which involved recruiting highly esteemed speakers, ensuring 50/50 gender balance, and consistently applying for and receiving funding from *The Physiological Society*.

(2) He has been highly active in promoting the careers of early career researchers (ECRs). For example, he has been the department's Postdoctoral and Research Staff Adviser since 2015 and in 2018 was appointed as the Academic Lead for ECRs across the entire College of Life Sciences giving him responsibility for supporting postdocs, fellows, and assistant professors across the College. Among the activities he has spear-headed as part of this role are securing internal funding for postdocs to conduct independent research, forming a postdoc and research staff association, supporting and mentoring fellowship applications, and delivering training workshops on funding, career progression, and work-life balance.

(3) He has been the university's representative for *The Physiological Society* since 2015. This role has included promoting membership of *The Society* to researchers from undergraduate students through to faculty, applying for funding for events and outreach activities, and attending meetings with society representatives from around the country facilitating transfer of information.

(4) He has been appointed to committees for the organization two prestigious international conferences: the Program Committee for the Society for the Study of Ingestive Behavior (2017-2020) and the Scientific Advisory Board of the International Society for Monitoring Molecules in Neuroscience (2018-2022).

(5) He has been invited to present at many internationally established conferences with highlights being the Presidential Symposium of Society for the Study of Ingestive Behavior (Seattle, 2014; a session devoted to promising junior faculty in the field of feeding), European Brain and Behavior Society (Verona, Italy, 2015), and an upcoming presentation at European Behavioural Pharmacology Society (Braga, Portugal, 2019). In addition, he has chaired numerous panels both as invited chair and as a result of proposing symposia.

(6) He has been an Academic Editor of *PLoS One* for four years and is currently Guest Editing a special issue of *Physiology & Behavior*. He regularly reviews for respected journals including *Science* and *Current Biology*.

(7) He has taken part in numerous outreach activities with highlights being (i) a newspaper article in *The Sun* (daily circ. ~1.6M) that won an award from the charity, *Understanding Animal Research*; (ii) a BBC/PBS television program, The Secrets of our Food; (iii) Brain Awareness Day events including talks and presentations from 2015 onwards; (iv) a public website, http://www.mccutcheonlab.com.

Progress towards Scientific Goals

The scientific objective of this project was to examine how the nutritional value of food (e.g. calories) affected neural activity in the mesolimbic pathway. The mesolimbic pathway is made up of dopamine neurons that release dopamine in the forebrain when they are active. It is known that these neurons have a role to play in feeding but it is not known exactly how sensitive they are to nutritional value. These possible interactions were described by Dr. McCutcheon in a review article in *Physiology & Behavior* (McCutcheon, 2015).

During the course of this project, the concept of nutritional value was broadened to encompass not just the energetic value of food (i.e. its calories) but also specific nutrients that all animals need to stay alive. One such nutrient is sodium and, in fact, in collaboration with his former lab in the US, Dr. McCutcheon showed that the dopamine system is sensitive to whether an animal needs sodium or not (Cone et al., 2016). In other words, rats that did not need sodium (sodium-replete) showed no dopamine release in response to infusions of sodium into the mouth whereas in rats in need of sodium (deplete), large dopamine response was seen to sodium infusions.

As well as sodium, Dr. McCutcheon's team has started investigating the role of another nutrient, protein, in determining food intake, palatability, and neural signaling. To this end, he recently published a paper showing that rats maintained on a low protein diet show increased preference for protein over carbohydrate (Murphy et al., 2018). In addition, another paper currently under review shows that this preference is associated with elevated activity in the dopamine-rich ventral tegmental area (Chiacchierini et al., *bioRxiv*).

As well as these principal projects, Dr. McCutcheon has collaborated locally in Leicester (Jones et al., 2015) and internationally with labs in Europe (Lutz Lab, Uni. Of Zurich; Whiting et al., 2017) and the US (Myers Lab, Bucknell University, USA: Naneix et al., *biorXiv*).

Dr. McCutcheon has attracted funding in addition to EU funds that supports work on similar projects:

- Role of nucleus accumbens in encoding nutritional value (BBSRC, UK; £456,085), 2015-2018.
- Neural and peripheral generation of a specific appetite for protein (Research Project Grant, The Leverhulme Trust; £194,257), 2018-2021.

Dr. McCutcheon has trained several group members including three postdoctoral researchers, two postgraduate students, and >10 undergraduates. The first of his PhD students completed her PhD in November 2018 and has started a postdoctoral position in the US (University of Maryland, Dr. Joseph Cheer

Selected publications since start of grant

McCutcheon (2015). *Physiol Behav* 152(Pt B):408-15.
Jones et al. (2015). *Front Behav Neurosci* 9:246.
Cone et al. (2016). *Proc Natl Acad Sci U S A* 113(7):1943-8.
Whiting et al. (2017). *Physiol Behav* 176:9-16.
Murphy et al. (2018). *Physiol Behav* 184:235-241.
McCutcheon & Roitman (2018). *ACS Chem Neurosci* [doi: https//doi.org/10.1021/acschemneuro.8b00262]
Hsu et al. (2018). *Front Psychiatry* 9:410.
Naneix et al. (2019). *bioRxiv* [doi: https://doi.org/10.1101/524272]
Chiacchierini et al. (2019). *bioRxiv* [doi: https://doi.org/10.1101/542340]