Parkinson's smell levels, symptom management and empowerment

When Joy met Alison

Joy Milne

Alison Williams

Alison Williams (PwP from Edinburgh) and Joy Milne first met in March 2016, where Joy placed Alison at a Level 3. When they met again eighteen months later Alison's PD odour had decreased significantly, to Level 1. Joy then sought — and got — ethical permission to talk to Alison about this observation.

Parkinson's and smell: Early work

The first paper to suggest a link between smell, sebum and Parkinson's was published by D Krestin in 1927: *The Seborrhoeic Facies as a Manifestation of Post-Encephalitic Parkinsonism and Allied Disorders*

Parkinson's and smell: Joy Milne

"My husband was a Consultant Anaesthetist and I was a nurse. 12 years before my husband was diagnosed his smell changed but it was not until we went to our first PD meeting that I realised everyone with Parkinson's had the same smell. As a doctor and a nurse we realised how important this discovery was. I approached the researchers at the Scottish Centre for Regenerative Medicine in Edinburgh, and we ran a small pilot test, which was 100% successful, opening the way to further examination."

Since 2012 Joy has been working with Professor Perdita Barran and her team at Manchester University to identify the molecules that make up the Parkinson's smell. The results have been published as: *Discovery of volatile biomarkers of Parkinson's disease from sebum*. Trevidi et al (2019)
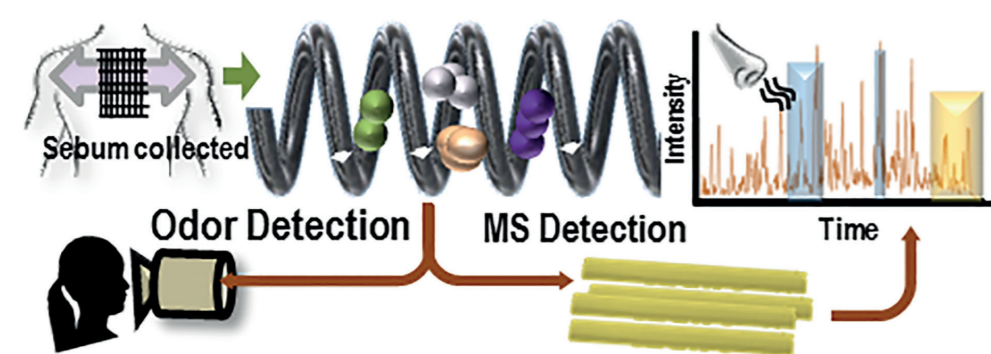
Identifying the molecules

Figure 1: Diagram of Analytical Method TD-GC-MS Analysis

Separation and identification of volatile biomarkers was achieved using a technique called Thermal Desorption Gas Chromatography Mass Spectrometry – TD-GC-MS.

Gauze that had been wiped on the upper back of participants is placed in a glass tube which is heated to release the volatile molecules. These are then separated on the GC column and passed to the mass spectrometer where they are weighed. The time each molecule spends on the column and its mass gives an identity.

The instrument as a 'T' piece before the mass spectrometer leading to an odor post which allows Joy to smell the molecules as they pass.

Parkinson's and smell: Stratification

Joy describes five different levels of smell, in which the individual person with Parkinson's (PwP) intrinsic smell moves from being predominant, to being overwhelmed by the musk smell of the Parkinson's sebum.

Level 1
The smell of the person. Therefore have to find the required molecules if they are there.

Level 2
Less of the person, more sebum musk smell. Easier to identify that the PD molecules are present

Level 3
Very little of the person, mostly sebum musk smell. Can smell the PD immediately but have to make an assessment of whether there is a high or low concentration of molecules.

Level 4
No person – a very strong sebum musty smell

Level 5
Putrescence – rancid and nauseous

Parkinson's and smell: Ethics

Joy's work is governed by very strict ethical guidelines. She will not tell anyone what she smells – neither whether they have Parkinson's in the first place, nor what level their smell is.

Impact and significance

Monitoring the scent of Parkinson's Disease could provide direct feedback to the PwP relating to their physical, cognitive and emotional states. We show here how this can develop self-awareness which allows the PwP to alter their behaviour in order to decrease the debilitating effects of this disease. This enhanced awareness has enabled Alison to actively modify behaviours: for example increasing exercise intensity or frequency, changing diet, or changing circumstances, particularly to manage or avoid stress.

"Exercise: the drug that is available to everyone"
Prof. Giovanna Mallucci (Sept 2018)

Developing Self Awareness

Joy has worked with Alison to help her to connect the odor level with her well-being. Knowing what each level feels like, physically, cognitively and emotionally, has enabled Alison to take more control over her own wellness. This self-monitoring gives Alison immediate awareness of how her symptoms are altering which can be constructively used alongside input from healthcare professionals.

Outcomes

Over the past two and a quarter years (Jan 2017 – April 2019) Alison has observed her motor and non-motor symptoms and has noticed significant changes.

Improvements:
- Sense of smell restored to 80% of pre-Parkinson's level
- Mood now consistently good, with little or no apathy
- Arm swing now happening unconsciously 80% of time
- Left-right coordination good and mostly (90%) unconscious
- Time-keeping with dance and drumming restored to accuracy
- Gait good 70%-80% of the time: length and speed of stride
- Physical multi-tasking restored to 80% (e.g. putting on gloves when walking down the street)
- Energy levels up by approximately 30%
- Dystonia in right foot completely gone
- Right leg resting tremor frequency reduced by 80%, except when triggered by adrenalin

Maintenance:
- Cognitive capacity (writing papers, presentations etc) maintained
- Voice volume maintained

No change (but no degeneration):
- Bladder urgency
- Poor short-term memory
- Turning in, and getting in and out of, bed
- Disturbed REM sleep

Implications for the future

The Trevedi paper (Trevedi et al 2018) concludes that this work, extending sebum biomarkers beyond diagnosis, can now examine stratification.

Future Work:
- To determine the distinguishing physical, cognitive and emotional features at each smell level and disease state, and to stratify these across PwP
- To understand how the smell levels change in response to intense, complex exercise
- To allow each individual PwP to use this approach to develop awareness of their disease and to adapt this for their own benefit, e.g. to optimise their own exercise and diet regime

As well as the diagnostic benefits, there is significant potential for increased effectiveness in symptom management, greater empowerment, and more accurate assessments of interventional impact.
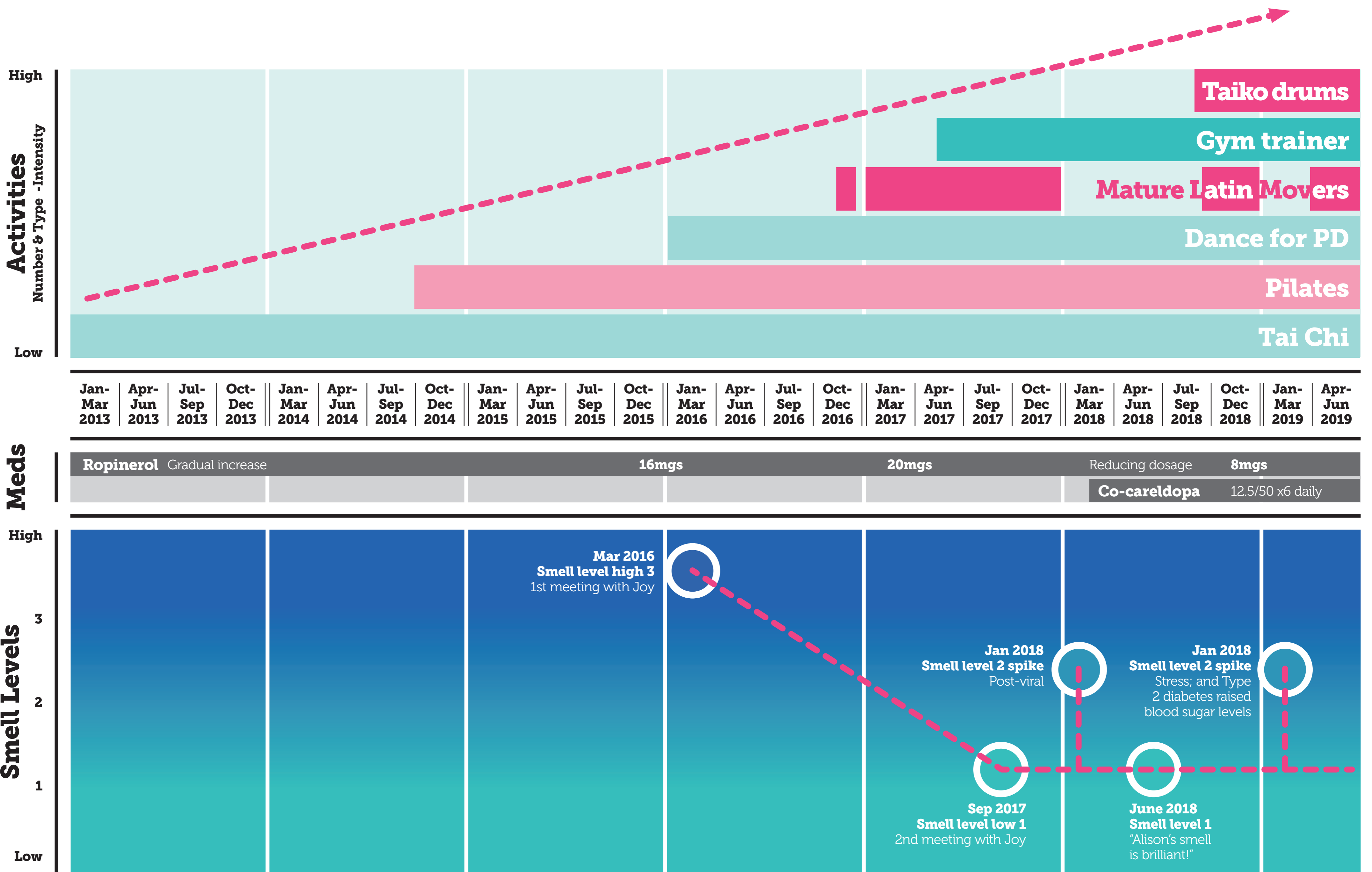
Acknowledgments

We are forever indebted to Tilo Kunath of SCRM for taking seriously the idea that Joy actually could smell Parkinson's, and for starting her – and the rest of the Parkinson's community – on this extraordinary adventure.

Our heartfelt thanks to Professor Perdita Barran, Dr. Monty Silverdale and their team at Manchester University (Drupad K. Trivedi, Eleanor Sinclair, Yun Xu, Depanjan Sarkar, Caitlin Walton-Doyle, Royston Goodacre) for their work with Joy, and for their generous support of this poster.

We thank designer Alan Tait for his patience and inventiveness in taking our initial ideas and making design sense of them.

Finally, we dedicate this poster to the memory of Les Milne, PwP extraordinaire, without whose courage, tenacity and sheer bloody-mindedness, all this might not have happened.

Activities
Number & Type – Intensity

(High to Low)

- Taiko drums
- Gym trainer
- Mature Latin Movers
- Dance for PD
- Pilates
- Tai Chi

Jan-Mar 2013	Apr-Jun 2013	Jul-Sep 2013	Oct-Dec 2013	Jan-Mar 2014	Apr-Jun 2014	Jul-Sep 2014	Oct-Dec 2014	Jan-Mar 2015	Apr-Jun 2015	Jul-Sep 2015	Oct-Dec 2015	Jan-Mar 2016	Apr-Jun 2016	Jul-Sep 2016	Oct-Dec 2016	Jan-Mar 2017	Apr-Jun 2017	Jul-Sep 2017	Oct-Dec 2017	Jan-Mar 2018	Apr-Jun 2018	Jul-Sep 2018	Oct-Dec 2018	Jan-Mar 2019	Apr-Jun 2019

Meds

Ropinerol — Gradual increase — 16mgs — 20mgs — Reducing dosage — 8mgs

Co-careldopa — 12.5/50 x6 daily

Smell Levels

(High, 3, 2, 1, Low)

Mar 2016
Smell level high 3
1st meeting with Joy

Jan 2018
Smell level 2 spike
Post-viral

Jan 2018
Smell level 2 spike
Stress; and Type 2 diabetes raised blood sugar levels

Sep 2017
Smell level low 1
2nd meeting with Joy

June 2018
Smell level 1
"Alison's smell is brilliant!"

References 1. Trivedi, D. K.; Sinclair, E.; Xu, Y.; Sarkar, D.; Walton-Doyle, C.; Liscio, C.; Banks, P.; Milne, J.; Silverdale, M.; Kunath, T.; Goodacre, R.; Barran, P. Discovery of volatile biomarkers of Parkinson's disease from sebum. ACS Cent. Sci. 2019, in press / 2. Krestin, D. The Seborrhoeic Facies as a Manifestation of Post-Encephalitic Parkinsonism and Allied Disorders. QJM 1927, os-21 (81), 177– 186, DOI: 10.1093/qjmed/os-21.81.177 / 3. What is Life? Paul Davies, Professor of Physics, Arizona State University, Tempe. New Scientist, 2nd February 2019. / 4. Bowie, D. (2018) Shared and unique aspects of ligand- and voltage-gated ion-channel gating. Editorial from *Journal of Physiology* 596.10 (2018) pp1829-1832. Ed: Ole Peterson. / 5. Bottions P., Tranchita E., Sansone,P. & Parisien A. (2014). Effects of physical activity in Parkinson's disease: A new tool for rehabilitation. *World Journal of Methodology*. 2014 Sep 26. / 6. Lau Y.S., Patki G., Das-Panja K., Le W-D. & S. Omar A. (2011) Neuroprotective effects and mechanisms of exercise in a chronic mouse model of Parkinson's disease with moderate neurodegeneration. *European Journal of Neuroscience* 2011 Apr, 33(7): 1264–1274.

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