Research over the past two decades has explored the role of immune processes in a range of mental health conditions, and has shown that pro-inflammatory cytokines, which promote systemic inflammation, can act as neuromodulators, orchestrating immunological and behavioural changes associated with depression [1]. Patients with depression exhibit decreases in cytokine levels proportionate to their degree of recovery when treated either with pharmacotherapy, psychotherapy or a combination of both [2].

In recent years, a number of programmes have developed across the UK and internationally providing psychosocial interventions such as yoga and mindfulness to improve symptoms of mental health conditions and reduce inflammatory response [3], [4]. One promising psychosocial intervention is music, and a recent systematic review identified over 60 studies showing the immune-modulating effects of a range of music interventions [5]. However, to date, music interventions have not been researched as inflammatory-reducing therapeutic agents in mental health.

Consequently, the current pilot study was designed to test the feasibility of using music interventions in mental health. The study explored the effects of group drumming on a broad array of inflammatory measures over a six week intervention. Drumming was selected as the music intervention because the inclusiveness of drumming circles, lack of fine motor skill requirement and strong steadying rhythms suggest that it <u>might-may</u> be particularly suitable in mental health settings. Furthermore, two previous short studies (single drumming sessions) involving healthy participants found changes in biological response [6], [7].

We hypothesised (i) a decrease in depressive symptoms, pro-inflammatory activity and cortisol along with an increase in wellbeing across the entire six-week intervention; (ii)- an increase in positive affect and immune-enhancing activity and a_decrease in cortisol after a single session.

To test these hypotheses, in the week preceding and following the six week intervention, participants completed psychological scales including the Hospital and Anxiety Depression Scale (HADS), the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS), the Connor-Davidson Social Resilience Scale (CD-RISC) and the Secker Scale for social inclusion. Immediately before and after the first and final sessions of the six-week intervention, participants provided a saliva sample, collected via passive drool method and stored immediately at -20*C. Recent research has documented the promise of salivary measurement in psychobiological research as a non-invasive, pain-free tool [8]–[10]. Saliva samples were analysed using Luminex multiplex assays. Furthermore, before and after the final session, participants completed visual analogue mood scales and blood pressure and heart rate measurements were taken.

Thirty-one adults with affective disorders categorised as 'mild' or 'moderate' on HADS took part in the study (8 men and 23 women; mean age \pm SEM: 52.8 \pm 2.45 years), recruited from hospitals, mental health professionals and support organisations and charities operating in West London. As this was a preliminary study, participants were recruited with a range of mild and moderate mental health conditions. Exclusion criteria included severe anxiety or depression (HADS>15), a confounding comorbidity or use of steroid or immunosuppressive medication. Participants took part in 90-minute group drumming sessions in groups of 15-20 over a period of six weeks. Sessions consisted of call-and-response exercises and learning drumming patterns that built up into larger pieces.

We used repeated measures ANOVAs to test changes in subjective reports and immune measures across individual sessions and the whole intervention. Corrections for multiple comparisons were made using Simes' Test, and all p values presented are corrected. We tested whether age and sex affected the observed differences in outcomes, but since they had no effect, we did not control for these variables in the final models.

Results are shown in Table 1. Across the entire intervention, significant improvements were found for depression, wellbeing and social resilience. From the beginning to the end of a single session, ratings of stress and tiredness levels significantly decreased, and happiness, relaxation and energy levels increased (all p<0.002, data not shown).

Across the entire intervention, the concentrations of four cytokines were significantly lowered, demonstrating a reduction of pro-inflammatory response. There was no evidence of a decrease in cortisol. From the beginning to the end of session 1, the concentration of four cytokines significantly increased, and from the beginning to the end of session 6, seven cytokines significantly increased and cortisol decreased. To test this difference in response noted between week 1 and week 6, we compared change scores calculated by subtracting the scores before a drumming session from scores after the same drumming session. This was only carried out for a subset of 13 participants who had provided viable saliva samples above the level of detection at both time points in session 1: IL-2 (p = 0.013), IL-6 (p = 0.021), IFN- γ (p < 0.001) and cortisol (p = 0.001). It is possible that responses during the first session were confounded by the anxiety of being in an unusual location with new people doing an unfamiliar activity. Or alternatively, participants may have become more responsive to the intervention as the weeks progressed.

Blood pressure was not reduced although there was a decrease in heart rate of 5.85bpm (p=0.003). Measures were taken immediately after sessions, and it is possible that greater effects would have emerged over a longer period.

This study demonstrated for the first time that group drumming for affective disorders can lead to reductions in cortisol and immune-enhancement over individual sessions, as well as reduce inflammatory activity over a six-week span. Changes in biomarkers are supported by changes in psychological profiles of participants, demonstrating the potential of group drumming as an intervention for mental health. This supports the undertaking of further controlled studies to test fully the therapeutic potential of group drumming interventions and other music-based psychosocial interventions for mental health patients.

References

- [1] C. L. Raison and A. H. Miller, "Is depression an inflammatory disorder?," *Curr. Psychiatry Rep.*, vol. 13, no. 6, pp. 467–475, Dec. 2011.
- [2] J. Dahl, H. Ormstad, H. C. D. Aass, U. F. Malt, L. T. Bendz, L. Sandvik, L. Brundin, and O. A. Andreassen, "The plasma levels of various cytokines are increased during ongoing depression and are reduced to normal levels after recovery," *Psychoneuroendocrinology*, vol. 45, pp. 77–86, Jul. 2014.
- [3] G. M. Slavich and M. R. Irwin, "From Stress to Inflammation and Major Depressive Disorder: A Social Signal Transduction Theory of Depression," *Psychol. Bull.*, vol. 140, no. 3, pp. 774–815, May 2014.
- [4] A. K. Forsman, J. Nordmyr, and K. Wahlbeck, "Psychosocial interventions for the promotion of mental health and the prevention of depression among older adults," *Health Promot. Int.*, vol. 26, no. suppl 1, pp. i85–i107, Dec. 2011.
- [5] D. Fancourt, A. Ockelford, and A. Belai, "The psychoneuroimmunological effects of music: A systematic review and a new model," *Brain. Behav. Immun.*, vol. 36, pp. 15–26, Feb. 2014.
- [6] B. B. Bittman, L. S. Berk, D. L. Felten, J. Westengard, O. C. Simonton, J. Pappas, and M. Ninehouser, "Composite effects of group drumming music therapy on modulation of neuroendocrine-immune parameters in normal subjects," *Altern Ther Health Med*, vol. 7, no. 1, pp. 38–47, Jan. 2001.
- [7] M. Koyama, M. Wachi, M. Utsuyama, B. Bittman, K. Hirokawa, and M. Kitagawa, "Recreational music-making modulates immunological responses and mood states in older adults," *J Med Dent Sci*, vol. 56, no. 2, pp. 79–90, Jun. 2009.
- [8] D. C. Slavish, J. E. Graham-Engeland, J. M. Smyth, and C. G. Engeland, "Salivary markers of inflammation in response to acute stress," *Brain. Behav. Immun.*, vol. 44C, pp. 253–269, Feb. 2015.
- [9] S. Williamson, C. Munro, R. Pickler, M. J. Grap, and R. K. Elswick, "Comparison of Biomarkers in Blood and Saliva in Healthy Adults," *Nurs. Res. Pract.*, vol. 2012, p. e246178, Apr. 2012.
- [10] M. L. Byrne, N. M. O'Brien-Simpson, E. C. Reynolds, K. A. Walsh, K. Laughton, J. M. Waloszek, M. J. Woods, J. Trinder, and N. B. Allen, "Acute phase protein and cytokine levels in serum and saliva: a comparison of detectable levels and correlations in a depressed and healthy adolescent sample," *Brain. Behav. Immun.*, vol. 34, pp. 164–175, Nov. 2013.

Table 1 Psychological and biological results								
	Session 1		$-\mathbf{F}(\mathbf{n})$	n c, e	Session 6		F (n)	Dc
	Before	After	F (II)	P	Before	After	F (H)	1
Psychological scales (across the six weeks) – mean (s.d.)								
HADSA	9.3 (4.2)					8.3 (3.9) ^e	2.80 (30) ^d	0.105
HADSD	6.3 (3.4)					4.5 (3.1)	9.76 (30)	0.007
CD-RISC	60.3 (16.5)					66.4 (17.4)	4.70 (31)	0.048
Secker	37.5 (7.8)					38.4 (7.4)	0.74 (31)	0.330
WEMWBS	44.6 (11.1)					49.7 (9.0)	9.61 (31)	0.007
Biomarkers (across the six weeks) – mean (s.d.) pg/mL								
IL-2	1.86 (0.56) ^d				1.63 (0.79)		1.00 (14)	0.378
IL-4	0.78 (0.58)				0.54 (0.44)		2.85 (16)	0.168
IL-6	0.44 (0.36)				0.16 (0.17)		9.94 (15)	0.027
IFN-y	2.00 (0.75)				1.34 (0.65)		9.13 (16)	0.027
TNF-α	1.66 (0.38)				1.47 (0.28)		7.01 (18)	0.038
MCP-1	2.78 (1.52)				2.28 (1.49)		10.06 (18)	0.027
TGF-β	0.45 (0.32)				0.40 (0.32)		0.285 (17)	0.601
Cortisol ^a	4.52 (1.82)				5.17 (1.87)		1.87 (18)	0.243
IL-10 ^b	10/15 (67%)				6/15 (40%) ^c			0.168
Biomarkers (across individual sessions) - mean (s.d.) pg/mL								
IL-2	1.76 (0.64) ^d	1.93 (0.79)	2.11 (26)	0.318	1.67 (0.81) ^d	2.30 (0.78)	9.53 (14)	0.016
IL-4	0.62 (0.43)	0.97 (0.68)	11.22 (24)	0.047	0.43 (0.19)	1.00 (0.67)	7.57 (12)	0.024
IL-6	0.36 (0.31)	0.41 (0.34)	0.63 (23)	0.639	0.15 (0.18)	0.44 (0.31)	12.34 (13)	0.011
IFN-y	1.63 (0.79)	1.95 (0.89)	8.43 (24)	0.047	1.25 (0.68)	2.22 (0.69)	24.12 (13)	0.004
TNF-α	1.57 (0.36)	1.69 (0.43)	3.31 (25)	0.288	1.43 (0.25)	1.72 (0.39)	10.71 (16)	0.011
MCP-1	2.41 (1.28)	2.70 (1.41)	2.13 (25)	0.047	2.03 (1.31)	2.61 (1.19)	6.08 (14)	0.032
TGF-β	0.40 (0.27)	0.60 (0.47)	10.13 (27)	0.036	0.36 (0.29)	0.58 (0.35)	4.13 (15)	0.061
Cortisol ^a	4.74 (1.40)	4.72 (1.72)	0.00 (28)	0.952	5.32 (1.72)	3.84 (2.70)	11.00	0.011
IL-10 ^b	17/25 (68%)	16/25 (64%)		0.803	4/13 (31%)	9/13 (69%)		0.024

HADSA: Hospital Anxiety Scale, HADSD: Hospital Depression Scale, CD-RISC: Connor-Davidson Social Resilience Scale, WEMWBS: Warwick-Edinburgh Mental Wellbeing Scale, IL: interleukin, IFN: interferon, TNF: tumour necrosis factor, MCP: monocyte chemotactic protein, s.d.: standard deviation. ^a nmol/L

^b More than 50% of the values of IL-10 were not detectable, so the variable was dichotomised as detectable or not detectable and analysed using McNemar's Test.

^c% detectable of total ^d Lower number due to missing data ^e Data collected the week proceeding the study