Anhedonia Behavioural Activation and Ketamine Therapy (AAKT): Shaping a Proposal With Patient and Public Involvement

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Aims: Ketamine and behavioural activation (BA) reduce levels of anhedonia in major depressive disorder (MDD), though neither resolves anhedonia. Combining these treatments could yield additive or even multiplicative benefits.

This poster summarises the development of a PhD fellowship proposal, discussing: (1) the initial patient and public involvement (PPI) interviews, exploring views on participation in ketamine research; (2) the resulting proposal, assessing the feasibility of a trial augmenting BA with IV ketamine for MDD and anhedonia.

Methods: 1. One-to-one PPI interviews were conducted with seven participants from a previous study of ketamine in treatment-resistant depression. Questions addressed (a) volunteering reasons, (b) positives to retain and areas to improve and (c) research objectives opinions.

2. Participants with MDD and anhedonia will be recruited from the community and local primary care services (GP and NHS Talking Therapies). A planned feasibility parallel-group randomised controlled trial will compare IV ketamine with BA (n=20), against midazolam with BA (n=20). Participants will attend eight visits (including one-month follow-up) over 10–12 weeks, receiving 3 ketamine or midazolam infusions in between 6 BA sessions. Feasibility of study procedures and collection of outcome measures will be assessed.

Results: A key motivator for participants to volunteer was hope that ketamine would improve depression symptoms. Some were curious about ketamine's effects. They wished to support research into depression treatments.

Most participants experienced a stark difference between ketamine and midazolam (placebo). They described feeling more open, malleable and involved in the world after ketamine.

Participants suggested future studies retain a focus on treating participants as individuals rather than a 'number' and allowing unrushed sessions. They thought clinician-led interviews helped reflect on symptom changes.

Participants found the consent process thorough. However, some suggested it should be clearer that mood changes from ketamine may not last. They recommended providing audiovisual materials on the ketamine experience/infusion room to support preparation. They suggested a check-in between infusion sessions and a final session to discuss onward referrals, medication advice and signposting to low-cost counselling and integration groups.

Most thought ketamine could enable better use of therapy time and that therapy could help make sense of thinking changes post-ketamine. Other suggestions for research included duration of symptom relief post-ketamine, treatment accessibility including in primary care, and medication side effects.

Conclusion: PPI interviews supported combining ketamine with psychotherapy. They provided key insights on improving study procedures to support research into augmenting primary care therapies for depression treatment.

Abstracts were reviewed by the RCPsych Academic Faculty rather than by the standard *BJPsych Open* peer review process and should not be quoted as peer-reviewed by *BJPsych Open* in any subsequent publication.

Dementia With Lewy Bodies: A Review of Disease-Modifying Therapies for α-Synucleinopathies

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Aims: The global demographic transition has led to a growing ageing population. Neurodegenerative disease prevalence is high in the elderly, as aged brains accumulate molecular and cellular damage. Protein misfolding and aggregation are pathological processes underlying neurodegeneration, as seen in dementia. This coupled with oxidative stress, disrupted ubiquitin-proteosome system and neuroinflammation may contribute to neuronal damage/death. Lewy Body dementia (LBD) collectively refers to Parkinson's disease (PD), Parkinson-disease dementia and dementia with Lewy bodies (DLB). It is characterised by Lewy Body (LB) deposits in the central nervous system, predominantly compromised of misfolded α-synuclein protein. Disease-modifying therapy (DMT) targets underlying protein misfolding and promotes LB clearance.

To review international trials on DMT safety, tolerability and efficacy in DLB.

To consider the molecular basis for protein misfolding and DMT in DLB.

Methods: Two international registries (ClinicalTrials.gov; EU clinical trials register) were consulted to identify agents being tested in completed, ongoing and recruiting trials. Both databases were searched by disease "Lewy body dementia" or "LBD" or "alpha-synuclein pathology" and study type "interventional" for phase I–III trials. Trials solely investigating diagnostic biomarkers, approved symptomatic DLB treatment or PD without dementia symptoms were excluded from final analysis.

Results: 11 trials were found studying DMTs for DLB. 10 out of the 11 trials were in phase II and one in phase I. The main agents investigated were tyrosine-kinase inhibitors (TKIs), phosphodiesterase-9 inhibitors, β-adrenergic agonists, and β GCase chaperones. Primary and secondary outcome measures were "safety/tolerability of agent", "changes in cognitive function" or "changes in serum/CSF α synuclein levels". Results from a phase I trial demonstrated a 3.85 and 3.5-point increase in mini-mental state examination scores at 6 months with nilotinib doses 300 mg and 150 mg, respectively. Contrastingly, only slight reduction in CSF/plasma α-synuclein was observed. Phase II trials for bosutinib versus placebo showed no significant difference in cognitive function. Trials for ambroxol, a β-GCase enzyme enhancing inhibitory chaperone, remain in recruiting stages but have proven drug tolerability due to fewer side effects. Data on CSF biomarker changes in DLB was unavailable.

Conclusion: Current understanding of protein misfolding in α-synucleinopathies suggests that a single DMT may be insufficient in