

partial agonist and κ -antagonist) and SAM (a sublingually bioavailable μ -opioid antagonist), is an investigational opioid system modulator for depression. BUP/SAM has shown efficacy versus placebo as an adjunctive treatment for major depressive disorder (MDD) and a consistent safety profile in previously reported, placebo-controlled clinical studies.^{1,2}

STUDY OBJECTIVE(S):

1. To characterize the safety profile following long-term treatment with BUP/SAM
2. To explore depression symptoms and remission rates in patients with MDD following long-term treatment with BUP/SAM

METHODS: FORWARD-2 (Clinicaltrials.gov ID: NCT02141399) enrolled patients who had participated in 1 of 4 controlled studies as well as de novo patients. All patients had a confirmed diagnosis of MDD, had a history of inadequate response to standard antidepressant therapies (ADTs), and had been treated with an adequate dose of an established ADT for ≥ 8 weeks before BUP/SAM initiation. ADT dosage could be titrated, but the ADT could not be changed. During the study, patients received open-label, sublingual BUP/SAM 2 mg/2 mg as adjunctive treatment for up to 52 weeks. Safety (primary objective) was assessed via adverse events (AEs), vital signs, laboratory analytes, and electrocardiography. Suicidal ideation or behavior (SIB) was evaluated by the Columbia Suicide Severity Rating Scale. Abuse potential, dependence, and withdrawal were assessed by AEs and the Clinical Opiate Withdrawal Scale. Exploratory efficacy endpoints included mean Montgomery-Åsberg Depression Rating Scale (MADRS) scores and remission rate (MADRS ≤ 10).

RESULTS: Of 1454 total patients, 49% completed the 52-week study, 11% discontinued due to an AE, and 40% discontinued because of other reasons as of the interim data cutoff date (April 30, 2017). Most AEs were of mild/moderate severity. Serious AEs were reported in 3.2% of patients. AEs occurring in $\geq 10\%$ of patients were nausea, headache, constipation, dizziness, and somnolence. There was no evidence of increased risk of SIB with BUP/SAM. Incidence of euphoria-related events was low (1.2%). After abrupt discontinuation of BUP/SAM, there was little evidence of withdrawal. BUP/SAM was not associated with meaningful changes in laboratory or metabolic parameters or in bodyweight. The mean MADRS score decreased from 22.9 (± 9.7) at baseline to 9.8 (± 8.8) after 52 weeks. The remission rate at 52 weeks was 52.5%.

CONCLUSIONS: Long-term treatment with BUP/SAM did not reveal any new safety findings and confirmed

that the risk of abuse and dependence with BUP/SAM was low. BUP/SAM maintained an antidepressant effect for up to 52 weeks of treatment in patients with MDD.

Funding Acknowledgements: Alkermes, Inc.

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53

Computer Vision, Facial Expressivity and Schizophrenia: A Review

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ABSTRACT: Introduction: Facial expressivity in schizophrenia has been a topic of clinical interest for the past century. Besides the schizophrenia sufferers difficulty decoding the facial expressions of others, they often have difficulty encoding facial expressions. Traditionally, evaluations of facial expressions have been conducted by trained human observers using the facial action coding system. The process was slow and subject to intra and inter-observer variability. In the past decade the traditional facial action coding system developed by Ekman has been adapted for use in affective computing. Here we assess the applications of this adaptation for schizophrenia, the findings of current groups, and the future role of this technology.

MATERIALS AND METHODS: We review the applications of computer vision technology in schizophrenia using pubmed and google scholar search criteria of “computer vision” AND “Schizophrenia” from January of 2010 to June of 2018.

RESULTS: Five articles were selected for inclusion representing 1 case series and 4 case-control analysis. Authors assessed variations in facial action unit presence, intensity, various measures of length of activation, action unit clustering, congruence, and appropriateness. Findings point to variations in each of these areas, except action unit appropriateness, between control and schizophrenia patients. Computer vision techniques were also demonstrated to have high accuracy in classifying schizophrenia from control patients, reaching an AUC just under 0.9 in one study, and to predict psychometric scores, reaching pearson’s correlation values of under 0.7.

DISCUSSION: Our review of the literature demonstrates agreement in findings of traditional and contemporary assessment techniques of facial expressivity in schizophrenia. Our findings also demonstrate that current computer vision techniques have achieved capacity to differentiate schizophrenia from control populations and to predict psychometric scores. Nevertheless, the predictive accuracy of these technologies leaves room for growth. On analysis our group found two modifiable areas that may contribute to improving algorithm accuracy: assessment protocol and feature inclusion. Based on our review we recommend assessment of facial expressivity during a period of silence in addition to an assessment during a clinically structured interview utilizing emotionally evocative questions. Furthermore, where underfit is a problem we recommend progressive inclusion of features including action unit activation, intensity, action unit rate of onset and offset, clustering (including richness, distribution, and typicality), and congruence. Inclusion of each of these features may improve algorithm predictive accuracy.

CONCLUSION: We review current applications of computer vision in the assessment of facial expressions in schizophrenia. We present the results of current innovative works in the field and discuss areas for continued development.

57

Pareidolia as a Manifestation of Folie à Deux

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ABSTRACT: Introduction: The spreading of pareidolia, the visualization of one image inside another image, from one member of a couple to another one is seen in a subtype of folie à deux called folie imposée.

CASE STUDY: A 27 year old right handed male started having delusions two years prior to presentation. He experienced marked hallucinations in which he saw faces imbedded in clothing and demon-like faces that would appear in certain shades. During his visual hallucinations, “demonic-like angles would tell me how to get to heaven.” His pareidolia would be such that he would be looking at shadows on the walls or folds in clothing and see images within another. His fiancé, whom which he had been with for six years, also began to have pareidolia where she would be able to see facial images in furniture; for example, a chair would have an evil face or folds of

material would have a jagged, folded distortion. These persisted more prevalently when she was with him.

RESULTS: General physical examination: Hypopigmented skin. Mental Status Examination: Feelings of unreality, blunted affect, disorganized and pressured speech, flight of ideas. Thought process: abnormal with circumstantiality. Cranial Nerve Examination: Cranial Nerve 2: Visual acuity 20/70 OD, 20/50 OS. Retinal freckles OS. Cranial Nerve 3, 4, 6: bilateral tortuosity. Cranial Nerve 9, 10: deviated to right. Motor Examination: Drift test: right abductor digiti minimi sign. Cerebellar Examination: decrease amplitude to move left upper extremity. Finger to nose with dysmetria bilaterally. Reflexes: Brachioradialis: right 1+, left 3+. Biceps: right 1+, left 2+. Triceps: 2+ bilaterally. Knee Jerk: right: 2+ and pendular. Ankle Jerk: 3+ bilaterally.

DISCUSSION: Healthy pareidolia where images inside clouds or images of constellations and star formations is a zeitgeist of imagination which is more intense in some cultures than others. Folie à deux is a shared delusional disorder and folie imposée is a subtype when the dominant or principal person forms a delusion and imposes it onto the secondary or associate person. If folie imposée pareidolia is spread from one member of a couple to the other, it suggests that the second individual may be overly empathic to the first due to the dominating nature of the principal individual; the associate individual may be passive and submissive and thus accepting these visual perceptions more willingly. Alternatively, the associate individual could already have pareidolia of visual images which subliminally influenced the principal individual to have them, and can be misinterpreted as the opposite. In this patient, the dominant person had a multitude of different delusions but the delusion of pareidolia was the one which transferred to the associate. It is unclear as to why it was this that transferred as opposed to the other delusions and further investigation in this realm is warranted.

58

Case Report: Clinical Challenges in the Diagnoses and Management of Delirious Mania in a US Veteran with a Mental Health History of Bipolar Disorder

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