**Background:** It remains unclear whether neuroimaging can predict ECT response and whether structural changes associated with ECT explain its therapeutic efficacy. We aimed to identify neural predictors of ECT and the relationship between ECT-induced neural changes and clinical or neurotrophic factors.
**Methods:** Clinical outcome measures 1 week prior to ECT (T0), after the sixth ECT (T1), one week (T2), four weeks (T3) after the last ECT and 6 months after the last ECT (T4). Neuroimaging techniques at T0 and T2 (visual rating scales, manual segmentation of hippocampal volume (HV), voxel based morphometry (VBM), and at T0 only (white matter hyper intensities (WMH), 18F-flutemetamol PET imaging and advanced surface and shape-based methodology) combined with serum Brain Derived Neurotrophic Factor (sBDNF) at T0, T1, T2 and T3.
**Results:** 1. Structural MRI characteristics (visual rating), vascular burden or late-onset were not associated with response. HV, WMH and amyloid burden did not predict clinical outcome. 2. We observed right-hemispheric GMV increase in caudate nucleus, medial temporal lobe, insula and posterior superior temporal cortex. A correlation was found between increased GMV in caudate nucleus region and psychomotor change but no co-evolution between changes in mood, HV and sBDNF. We identified subcortical morphological changes with a weak relationship between striatum displacement and psychomotor function.
**Conclusions:** HV, WMH and amyloid load are not related to ECT response, suggesting ECT should be considered on clinical grounds regardless of markers of age-related brain pathology. Following ECT, structural changes are unrelated to changes in depressive symptomatology, suggesting a complex mechanism of ECT in LLD.
**Supported By:** Research Foundation - Flanders (FWO) (Dr. Vandenbulcke).
**Keywords:** Late Life Depression, Electroconvulsive therapy, Longitudinal Brain Imaging, Neural correlates

## 446. Predicting ECT Response with Baseline Neuroimaging Data

**Christopher Abbott**[1] and Jing Sui[2]

[1]University of New Mexico, [2]Mind Research Network

**Background:** Biological markers may be informative in identifying depressed patients who respond to a specific antidepressant treatment. Due to its rapid and robust clinical effects, electroconvulsive therapy (ECT) represents an optimal model to develop and test treatment biomarkers of eventual response.
**Methods:** Advanced pattern matching and data mining techniques identified structural magnetic resonance imaging (sMRI) networks predictive of recovery from depression from three independent data sets (UNM, n = 38; LIJ, n = 7; and UCLA, n = 10).
**Results:** For the UNM data set, six grey matter (GM) regions were repeatedly identified as predictive of future response (change in depression ratings) at r=0.90 and classified eventual remitters with high precision (sensitivity 88.9%, specificity 90.9%). We further tested these potential biomarkers using pre-ECT GM data from two independent, demographically-matched data sets from UCLA and LIJ; high estimation accuracy of eventual change in depression severity and predictive accuracy of remitter were also achieved (UCLA: r = 0.71, sensitivity 100%, specificity 87.5%; LIJ: r = 0.77, sensitivity 66.7%, specificity 100%). Two of the six extracted predictive regions (right supplementary motor/superior frontal and right post-central gyrus) showed GM volume changes over the four-week assessment interval; the remaining predictive regions (left hippocampal/parahippocampal, left inferior temporal, left middle frontal and right angular gyrus) did not vary significantly with treatment.
**Conclusions:** These results suggest a particular network of GM features can serve as a prognostic sMRI biomarker to guide personalized treatment decisions. Findings also suggest that antidepressant response involve interactions between treatment predictive and treatment responsive networks.
**Supported By:** NIMH 1R01 MH111826-01 and 2P20GM103472-01 (Abbott and Sui)
**Keywords:** Depression, Structural MRI, Electroconvulsive therapy, Prediction of Treatment Outcome, Machine learning

## 447. Establishing a Multi-Site Investigation of the Neural Mechanisms Underlying Response to Electroconvulsive Therapy

**Leif Oltedal**[1], Hauke Bartsch[2], Ole Johan Evjenth Sørhaug[3], Ute Kessler[4], Anders M Dale[2], Ketil J Oedegaard[3], and for GEMRIC[5]

[1]Center for Multimodal Imaging and Genetics, University of California, San Diego, [2]Center for Multimodal Imaging and Genetics, University of California, San Diego, [3]Department of Clinical Medicine, University of Bergen, [4]Division of Psychiatry, Haukeland University Hospital, [5]The Global ECT-MRI Research Collaboration

**Background:** It is unclear how structural and functional brain changes after ECT associate with stimulus parameters and clinical outcome. Larger studies accounting for individual differences in clinical and treatment parameters are necessary to target biological factors relating to or predictive of antidepressant response.
**Methods:** A systematic literature search identified contributing groups and the Global ECT-MRI Research Collaboration (GEMRIC) was formed. Methods for standardization of multi-site clinical data were established and a common data portal for mega-analysis developed. The image processing pipeline includes pre-processing with corrections for scanner specific distortions, FreeSurfer and unbiased estimates of regional anatomical change with Quarc.
**Results:** The GEMRIC data sample consists of 345 subjects (age range 19-86; ~ 60 % female, ~ 85% unipolar depression) from 14 sites with 2 - 4 imaging time points. The processing pipeline was evaluated on data from one site with two scanners. The effect sizes (Cohen´s d) of Quarc regional ECT-induced anatomical volume change were typically in the range 0.5 – 2. The pattern of change was broadly distributed and lateralized to the side of the stimulus; e.g. the volume of the right and left temporal pole regions changed by 4.9 ($p<0.0001$) and 2.6 % ($p<0.05$), respectively (n=19), compared to healthy controls (n=9).
**Conclusions:** Standardized image processing and statistical tools for analysis combined with the large and heterogeneous dataset will provide new opportunities to investigate factors mediating and predictive of clinical outcomes, which may

ultimately lead to more effective personalized treatment approaches.
**Supported By:** Western Norway Regional Health Authority, Haukeland University Hospital and the University of Bergen, Norway.
**Keywords:** ECT, Structural MRI, Longitudinal Brain Imaging, Major Depression

## SYMPOSIUM
## Bipolar Disorder with Comorbid Binge Eating Disorder – Validation of a Clinically Important Sub-Phenotype

Friday, May 19, 2017 - 3:00 PM - 5:00 PM
Aqua EF
Chair: Marin Veldic
Co-Chair: Susan McElroy

### 448. Evidence for a Role of Binge Eating and Obesity in Bipolar Disorder Genetic Risk: Genome-wide Associations in PRR5-ARHGAP8 and TCF7L2

**Alfredo Cuellar Barboza**[1], Susan McElroy[2], Stacey Winham[3], Colin Colby[3], Euijung Ryu[3], Miguel Prieto[4], Mark Frye[3], and Joanna Biernacka[3]

[1]UANL, [2]Lindner Center of HOPE/University of Cincinnati College of Medicine, [3]Mayo Clinic, [4]Universidad de los Andes

**Background:** Bipolar disorder's (BD) genetic architecture may be modified by interrelated heritable traits. For example adiposity-related traits, binge eating behavior (BE) and obesity, are positively associated with BD and compose complex subphenotypes of distinctive morbidity. We sought to perform genome wide analyses (GWA) of BD accounting for BE, body mass index (BMI) and BMI-gene interactions.
**Methods:** We conducted a BE GWA using 968 BD cases and 777 controls. We used logistic regression analyses comparing BD cases with and without BE, adjusted for 4 principal components. Top variants were assessed for replication in an independent population (N=1001). To investigate obesity, we used 388 BD cases and 1020 healthy controls with available BMI data. We performed GWAs of the genetic effects accounting for BMI, and SNP–BMI interactions. Results from the top finding of this GWA were replicated using an independent sample of 662 BD cases and 616 controls.
**Results:** For BE no variants reached genome-wide significance in the separate analyses. However, a meta-analysis provided genome-wide significant evidence of association with rs726170 (OR=1.91, P=3.05E-08) in a read-through gene PRR5-ARHGAP8 in BD case-only analysis. We found a genome-wide significant hit in rs12772424 (P=2.85E−8) an intronic variant in TCF7L2, with interaction effects that indicate that higher BMI confers higher BD risk in low allele carriers. This finding was independently replicated in the Mayo sample (P=0.011).
**Conclusions:** BE and obesity in BD are associated with common variants in read-through genes potentially related to feeding behavior and TCF7L2, the effector of the canonical Wnt signaling pathway, respectively.

**Supported By:** Marriott Family Foundation and Mayo Clinic's Center for Individualized Medicine.
**Keywords:** BMI, Binge Eating Disorder, Bipolar Disorder, GWAS

### 449. Preclinical Models for the Study of Binge Eating Disorder

**Michael Statnick**

Eli Lilly and Company

**Background:** Binge eating disorder (BED) affects roughly 1–4% of the U.S. population. BED is characterized by repeated episodes of eating unusually large amounts of food in a short period of time without engaging in compensatory behaviors. Preclinical animal models of BED have been developed employing caloric restriction and/or exogenous stressors to stimulate binge-like eating. We have developed a preclinical model of BED in mice that does not require caloric restriction or stress.
**Methods:** Mice were randomized according to body weight, and divided into one of three experimental groups; chow, continuous access, or intermittent access. Chow controls received unlimited access to a standard rodent chow diet. Continuous access animals had ad libitum access to both standard chow and a high energy diet (HED). The intermittent access group received standard chow ad libitum and HED for 24-h once weekly. For drug treatments, animals were randomized based on 2.5-hr HED intake and administered either vehicle, or drug (fluoxetine, baclofen, topiramate, or various opioid antagonists) in a dose volume of 1 mg/ml.
**Results:** Mice under the protocol exhibited a significantly elevated intake of HED on access days. The increased intake of HED was consistent across multiple bingeing cycles. Interestingly, opioid antagonists, fluoxetine and baclofen were all effective in reducing binge-like eating, while topiramate was not active.
**Conclusions:** Preclinical models exhibit many of the hallmark characteristics of BED. As known clinically efficacious compounds reduce binge-like eating in these rodent models, these may be useful in identifying novel pharmacological treatments for BED.
**Supported By:** Eli Lilly and Company
**Keywords:** Binge Eating Disorder, Rodents, Fluoxetine, Opioid system

### 450. In Bipolar Disorder, SLC1A2 Promoter Hypomethylation is Associated with Binge Eating Disorder and Nicotine Dependance

**Marin Veldic**[1], Yun-Fang Jia[2], YuBin Choi[2], Jennifer R Ayers-Ringler[3], Joanna M Biernacka[4], Jennifer R Geske[5], Susan McElroy[6], Mark Frye[1], and Doo-Sup Choi[7]

[1]Mayo Clinic, [2]Department of Molecular Pharmacology & Experimental Therapeutics, Mayo Clinic, Rochester MN, [3]2Neurobiology of Disease Program, Mayo Graduate School, Mayo Clinic, Rochester, MN, [4]Department of Psychiatry & Psychology, Mayo Clinic Depression Center; Division of Biomedical Statistics and Informatics, Mayo