Title slide

Martens – Pre-Print Paper Presentation. I selected that title because it was a challenge to pronounce so many “P”s. But that is fitting as most antipsychotics are a challenge to pronounce.

Slide 1

Thanks for coming everyone. I chose this paper for several reasons and I look forward to hearing your impressions and comments on whether this new classification system is beneficial to our work.

This is a new work from the authors who are amongst the top 100 cited researchers in this field. Classification systems for these drugs is not new and these researchers have published previously on a classification system using network analysis.

Slide 2 – Background

So the focus of the paper is on developing a new classification system for AP medications. What is special about this work is that:

1. Strives to bridge the gap between clinical and research domains – and create a system that maps onto both pharmacological and clinical effects - the focus for clinicians may not be as strong on mechanisms, while a greater understanding of txt effects or side effects may provide researchers with insight or evidence of the mechanisms under study.
2. Create a classification system that facilitates a switch to another medication to improve txt response and tolerability.
3. Clarify oversimplification (typical/atypical, 1st vs 2nd gen.). These terms do not provide necessary information and simplifications obscure important similarities and differences between drugs. This group has actually a highly diverse pharmacology.

Slide 3 Method: Research-focused data

Step 1: Determine AP receptor affinities

- Receptor affinities obtained from NIMH. (Psychoactive Drug Screening Program database.)

- Include receptor if data were available for ≤ 5 separate drugs.

- Include AP if data were available for ≤ 5 separate receptors.

- Remove receptors if Ki values were identical for all drugs.

- Convert Ki to pKi values.

Slide 4 Method: Research-focused data

Step 2: Cluster APs by receptor affinities

- Adjusted the pKi values for agonists or partial agonists at a given receptor.

- Create correlation matrix with adjusted pKi values.

- Group AP with similar receptor profiles into distinct groups.

Slide 5 Method: Research-focused data

Step 3: Characterize relationships - receptor profiles, other classification methods, and clinical effects

- Performed Probabilistic PCA and calculated the average contribution of each cluster to the first three PCs. This is the mean component loading.(which explains the greatest proportion of variance).

- Compare the ability of these clusters to predict side effects.

- Compare results to existing methods of categorizing Aps including Neuroscience based Nomenclature, basic receptor profile defined groupings and the atypical/typical/partial agonist groupings.

- Evaluated median absolute error for 27 APs.

Slide 6 Method: Clinical-focused data

- Created a database of side effects as recorded in The Maudsley

Slide 7 Results 1: Antipsychotic pKi values

Slide 8 Results 2: AP clustering based on receptor profiles

Slide 9 Results 3: Characterized receptor-defined AP clusters

Slide 10 Results 4: Characterized clinical profiles of PCs & receptor-defined clusters

Slide 11 Results 5: AP categorisation schemes & prediction of clinical effects

Slide 12. Conclusions

- Data driven method provides a system for researchers and clinicians.

- ID of 4 groups of 42 receptors and 27 APs that map well to clinical profiles.

- Groups 1 and 4 were more efficacious than clusters 2 and 3.

- Method has potential for personalized psychiatry

predicting side effects

groups 1 & 4 more efficacious than 2 & 3