**The *Movement* Disorder Society's**
**17th International Congress of Parkinson's Disease and Movement Disorders**
**Sydney, Australia**
**June 16-20, 2013**

**479**
**Title:** The lessebo effect in Parkinson's disease.

Tiago A. Mestre, MD MSc[1], Prakesh S. Shah[2], Connie Marras, MD PhD[1] and Anthony E. Lang, MD[1]. [1]Movement Disorders Centre and Edmond J. Safra Program in Parkinson's disease, Toronto Western Hospital, University Health Network. Division of Neurology, University of Toronto, Toronto, ON, Canada and [2]Department of Paediatrics and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada.

**Objective:** To assess the effect of the expectation of receiving placebo on the efficacy of antiparkinsonian drugs in Parkinson's disease (PD).

**Background:** In randomized controlled trials (RCTs), the use of placebo is standard. A patient's negative expectation of being given a placebo rather than an active treatment has been coined the lessebo effect, and is expected to underestimate the therapeutic potential of a drug being tested. The lessebo effect is opposite to the widely studied placebo effect and has never been considered or evaluated in movement disorders.

**Methods:** We conducted a systematic review of double blind RCTs of dopamine agonists in PD, using either placebo or an active treatment as control. We calculated the difference between the pooled effect size of the change of the UPDRS-III according to: 1) presence or absence of a placebo arm, 2) probability of placebo assignment (equal or < 50%). A random-effects model was used. An alpha $\leq 0.05$ was significant.

**Results:** 72 study arms of an active treatment were extracted from 39 RCTs: 30 from RCTs without a placebo arm (active comparator) (3391 PD patients), 42 from RCTs with a placebo arm (4554 PD patients). The between-group difference in the effect size of the UPDRS-III change was 1.75 units (95% CI 0.45-3.05; p=0.009), greater in studies with an active comparator. There was no difference according to the probability of placebo assignment. Subgroup analyses revealed that the lessebo effect was statistically significant only for study durations <3 months and in PD patients with shorter disease duration (<2.7 years), no motor fluctuations and a lower UPDRS-III score at baseline (<24 units).

**Conclusions:** We provide preliminary evidence that a placebo arm reduces the measured efficacy of an active treatment in RCTs in PD. The greater relevance of the lessebo effect in earlier disease stages and shorter duration studies has implications for study design and the interpretation of documented efficacy. The biological mechanisms underlying this effect require further study.