A growing body of research shows that cognitive remediation treatments involving neurofeedback can improve working memory in response to an extended (6-month), randomized, controlled trials (Kurtz et al., 2007; 2015) that revealed efficacious treatments. Richardson, 2005). This finding emphasizes the need of determining factors that predict a strong response to CR to effectively match patients to efficacious treatments.

**Methods:** We compared CT with and without pupillometry incorporated into the training algorithm in all three groups. While CT with and without pupillometry improved processing speed, greater gains were noted in the neurofeedback groups on both motorical and non-motorical processing speed. The neurofeedback groups, regardless of psychosis stage, also reported greater motivation/interest for treatment, with 90% completing the entire training compared to just 72% in the group without neurofeedback.

**Conclusions:** This shows that CT can be quite taxing for people at any stage of psychosis, and correct/incorrect responses do not fully gauge the level of cognitive resources one commits to a task. Pupil dilation betrays underlying physiologic engagement and serves as a precursor to disengagement on a behavioral task. We know that there is a “sweet spot” for the optimal load placed on cognitive resources, in terms of whether a training task is not stimulating enough (constricted pupils), ideally stimulating, or if there is too much information and the task has become overwhelming (dilated pupils). Pupillometry allows us to optimize the training exercises by providing biofeedback to the training software that then uses this information, along with task performance data, to automatically adjust training task parameters and levels for a personalized and efficient training program. In this manner, pupillometric neurofeedback can provide a concise index of how much the person is actively involved in the exercise at that very moment, even before performance can be registered as a correct or incorrect response.

**11.3 PREDICTORS OF RESPONSE TO COGNITIVE REMEDIATION IN SCHIZOPHRENIA**

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**Background:** A growing body of research shows that cognitive remediation (CR) consisting of drill-and-practice and/or strategy training targeted at neurocognitive functions produces small-to-moderate improvements in neurocognition that are durable and generalize to psychosocial function when CR is provided with other rehabilitation interventions (Wykes et al., 2015). Despite these positive group findings, results to date reveal substantial individual differences in response to CR interventions. For example, one summary of three CR trials found improvement rates for a mixed group of psychiatric patients that ranged between 40 and 69% for individuals (Medalia and Richardson, 2005). This finding emphasizes the need of determining factors that predict a strong response to CR to effectively match patients to efficacious treatments.

**Methods:** The current study is a secondary data analysis from two separate, randomized, controlled trials (Kurtz et al., 2007; 2015) that revealed improvements in working memory in response to an extended (6-month), standardized, computer-assisted cognitive remediation intervention when compared to an active, computer-skills control condition. We investigated the relationship between demographic factors (age, education, duration of illness), hours of CR treatment, cognitive skills (crystallized verbal ability, visual sustained attention, verbal learning and memory, and problem-solving), and symptoms (total positive and negative symptoms and general symptoms) measured at study entry, to improvements in working memory skills across these two RCTs.

**Results:** Results from 58 people with chronic schizophrenia randomly assigned to the CR condition in these two studies (mean age=34.1 years, SD=12.0; mean duration of illness=10.2 years, SD=10.3) revealed that baseline visual sustained attention (partial r=.30, p=.05) and number of hours of training (partial r=.27 p=.05) predicted end of trial working memory scores with baseline working memory scores held constant.

**Conclusions:** These findings will be evaluated with respect to other studies of prediction of response to CR.

**11.4 TOWARDS A MODEL FOR PERSONALIZING COGNITIVE REMEDIATION ON THE BASIS OF GENETIC POLYMORPHISMS**

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**Background:** Cognitive remediation (CR) for schizophrenia is an evidence-based intervention as it has been demonstrated in meta-analytic studies. However, little is known about how individual differences could be affecting responsiveness. Among other variables, genetic variability could help to understand some aspects of the underlying biological mechanisms of cognitive remediation in schizophrenia. Intuitively, genetic variability could be causing different responsivity to cognitive remediation and then, if that would be proved, variability in genetics could help to define new predictors of response and eventually they might allow us to personalize treatments in the near future.

**Methods:** In this talk we will discuss the literature on genetic factors that may impact response to CR and the results of a systematic review will be presented. Moreover, an exploratory study testing the potential role of two different gene polymorphisms (COMT and BDNF gene) on cognition in a sample of n=110 participants with schizophrenia will be presented. Finally, a tentative model for predicting responsiveness to CR will be presented.

**Results:** Two different genes have been studied in the context of CR responsiveness. The brain-derived neurotrophic factor (BDNF) has been proposed as a specific marker of cognitive recovery. When samples were divided according to the resulting polymorphisms of the BDNF gene, the carriers of the Met allele behaved totally differently from the rest and no increase in serum BDNF levels was observed, while those without the Met allele did experience an increase in serum levels similar to previous studies. Those data could be potentially reflecting the presence of a negative response marker to cognitive remediation. On the other hand, some studies have shown that other gene polymorphisms, especially those that influence the release of dopamine, could act to influence the response to cognitive interventions in schizophrenia. The most studied is catechol-O-methyltransferase (COMT), which is an important enzyme for the degradation process of dopamine that regulates the availability of dopamine in the frontal cortex. Finally, in our own sample significant differences were found in different COMT polymorphisms in cognitive flexibility (t= 12.81; p = 0.001). In addition, significant differences were also found in measures of verbal learning (t= 11.87; p = 0.04) for different variants of the BDNF gene.

**Conclusions:** Current data allow us to postulate a provisional model for predicting response to cognitive remediation including the BDNF Val66Met polymorphism and the COMT Val158Met polymorphisms. It seems like those polymorphisms could be accounting for different response to cognitive remediation in different cognitive domains: memory and cognitive flexibility. Eventually, if more new data about different genetic