# CEREBELLAR ATROPHY AFFECTS REWARD-BASED DECISION MAKING IN DM1 PATIENTS.

M. Bruschini<sup>1</sup>, L. Serra<sup>1</sup>, A. Petrucci<sup>2</sup>, G. Silvestri<sup>3</sup>, E. Bucci<sup>4</sup>, G. Antonini<sup>4</sup>, L. Licchelli<sup>4</sup>, B. Spanò<sup>1</sup>, M. Giancanelli<sup>2</sup>, C. Caltagirone<sup>5,6</sup>, M. Cercignani<sup>7</sup>, and M.Bozzali<sup>1</sup>.

1. Neuroimaging Laboratory, IRCCS Santa Lucia Foundation, Rome-Italy. 2. Neuromuscular and Neurological Rare Disease Centre, San Camillo-Forlanini Hospital, Rome-Italy. 3. Department of Geriatrics, Orthopaedic and Neuroscience, Institute of Neurology, Catholic University of Sacred Heart, Rome-Italy. 4. Department of Neurology, Mental Health and Sensory Organs (NESMOS), Faculty of Medicine and Psychology 'La Sapienza' University, Rome-Italy. 5. Department of Clinical and Behavioural Neurology, IRCCS Santa Lucia Foundation, Rome-Italy. 6. Department of Neuroscience, University of Rome 'Tor Vergata', Rome-Italy. 7. Brighton & Sussex Medical School, Clinical Imaging Sciences Centre, University of Sussex, Brighton-United Kingdom.

#### Introduction

Myotonic Dystrophy type 1 (DM1) is an inherited, multisystemic and progressive disease characterized by myotonia, muscle weakness, muscular dystrophy, endocrinopathy, cataract, cardiac conduction defect, and central nervous system dysfunctions [1]. DM1 patients show high-level cognitive deficits [1] including executive dysfunctions. Among them little is known about the decision making processes. Aim of this study was to investigate the relationship between reward-based decision-making ability and regional grey matter (GM) abnormalities in patients with DM1.

#### Methods

A cohort of 20 patients with molecular diagnosis of DM1 and a group of 16 healthy subjects entered the study. To assess the reward-based decision-making all participants underwent a computerized version of Iowa Gambling Task (IGT) [2], which provides scores for choices with a large immediate rewards, but long term losses (disadvantageous responses), and for choices with small immediate rewards, but long-term benefits (advantageous responses). A differential IGT score [d-IGT] (expressed as disadvantageous-advantageous responses) was also computed in DM1 patients and it was used in the further analyses. DM1 patients underwent MRI scanning at 3T, including T1-weighted volumes for voxel-based morphometry analysis, which was carried out in SPM8 using an optimized method. A regression model was used to investigate correlations between patients' d-IGT scores and changes in regional GM volumes.

#### Results

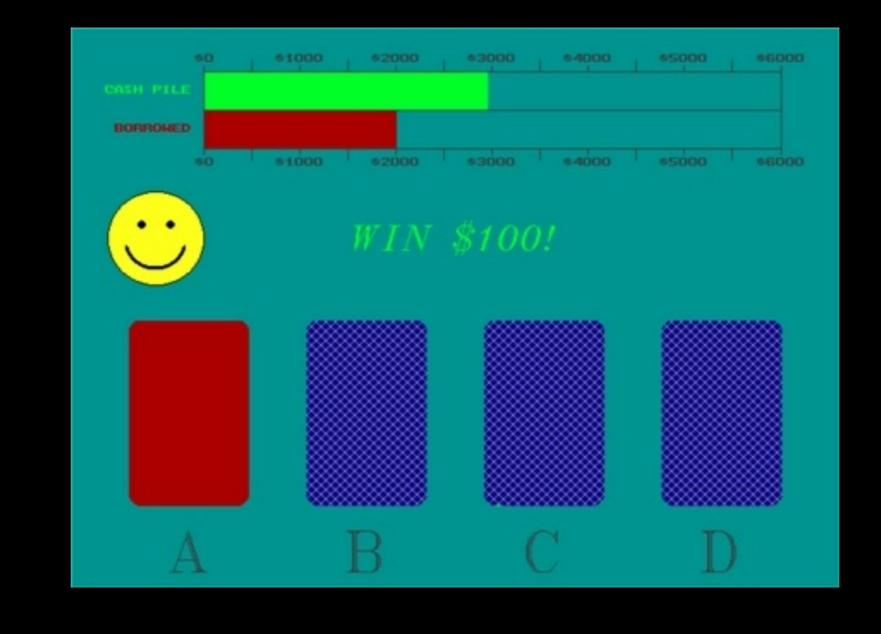
Neuropsychological results showed that DM1 patients were significantly worse than controls inidentifying advantageous responses. VBM analysis revealed a significant positive correlation between patients' d-IGT scores and regional GM volumes in the cerebellum (crus II), fusiform gyrus, cuneus/precuneus bilaterally, and in the left occipital pole.

#### Conclusions

This study reveals for the first time an impairment in reward-based decision making in patients with DM1. Moreover, this impairment in decision-making was significantly associated with reduced GM volumes in DM1 brains, including the cerebellum. As previously reported in other neurological diseases, the cerebellum is implicated in the ability of learning from experience [3], and might account for the difficulties experienced by DM1 patients in discriminating between advantageous and disadvantageous responses in the IGT, and in developing appropriate strategies to successfully run this task.

## References [1] Turner C., Hilton-Jones D., (2010). The myotonic dystrophies: diagnosis and management. Journal of neurology, neurosurgery, and psychiatry, 81; 385-367. [2] Bechara A., Damasio A.R., Anderson S., (1994). Insensitive to future consequences following damage to human prefrontal cortex. Cognition, 50 7-15. [3] Cardoso C. de O., Branco L.D., Cotrena C., Kristensen C.H., Schneider Bakos D.D., Fonseca R.P., (2014). The impact of frontal and cerebellar lesions on decision making: evidence from the Iowa Gambling Task. Front Neurosci, 8; 8-61

#### **Iowa Gambling Task (IGT)**

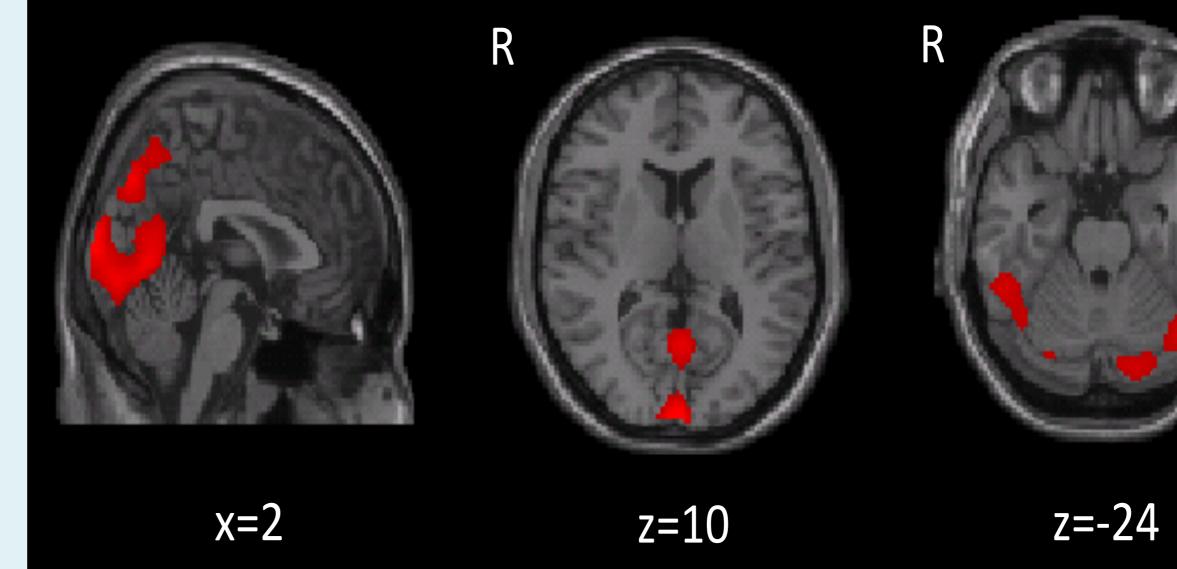


Trial of computerized version of IGT (Bechara et al, 1994).

The IGT is a neuropsychological measure that assess reward-based decision-making abilities. Using monetary choices, the task allows classification of the participant's performance in terms of aversion or risk taking. The task consists of four decks of cards of similar appearance (labeled A, B, C and D). The participant is told, during the initial verbal instructions, to select one card at a time from any of the fours decks. They are told that each time they choose a card they will win some money and that occasionally they will also lose some money. They are also told that the goal of the IGT is to win money, or maximize profit.

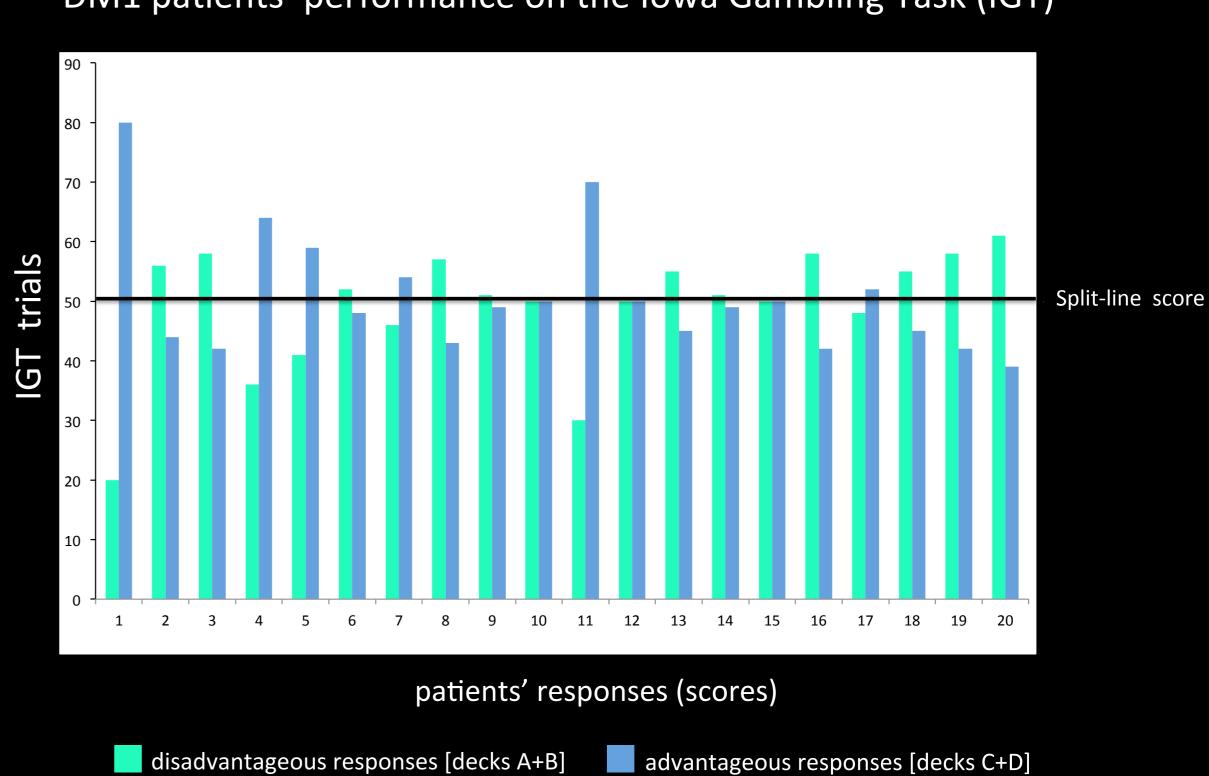
GM

### DM1<HS



Areas of reduced grey matter (GM) volumes in DM1 patients compared to control subjects group [p<0.05 FWE corr.] associated with impairment in reward-based decision-making abilities.

#### DM1 patients' performance on the Iowa Gambling Task (IGT)



Performance characterized by 50% of advantageous responses meet the criteria proposed by Bechara (*Bechara et al, 1994*) for a task successfully executed.

In our sample, 55% of patients DM1 did not performed correctly the task.