

A BEAUTIFUL MIND

THE 22Q11.2 MOUSE MODEL SHOW PARADOXICAL COGNITIVE IMPROVEMENTS IN TASKS OF LEARNING, MEMORY AND EXECUTIVE FUNCTIONING



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INTRODUCTION

The greatest current known risk factor for schizophrenia is the 22q11.2 chromosomal microdeletion. Here we present data from behavioural phenotyping of a 22q11.2 mouse model over a period of 20 months. The tests used all tap on neural structures and cognitive domains disrupted in schizophrenic and 22q11DS patients.

5-CHOICE SERIAL REACTION TIME TASK

This task has robust validity for modelling attentional impairments of psychiatric disease and performance is dependent on neural structures affected in 22q11DS patients and 22q11 mice (Ellegood et al. 2013)

TOUCHSCREEN AND T-MAZE DELAYED NON-MATCH TO LOCATION

Working memory is impaired in schizophrenic and 22q11DS patients and a 22q11.2 mouse model (Stark et al. 2008). Performance is mPFC- and hippocampal-dependent, where 22q11.2 mice show abnormalities.

REVERSAL LEARNING

Across species, performances in reversal learning is dependent on the OFC, a region altered in mice and patients carrying the mutation.

PAIRED-ASSOCIATE LEARNING (PAL)

The PAL-task measures object in place learning which is impaired in 22q11DS patients (Bearden et al. 2001). Task performance is dependent on hippocampal and medial prefrontal cortical regions.

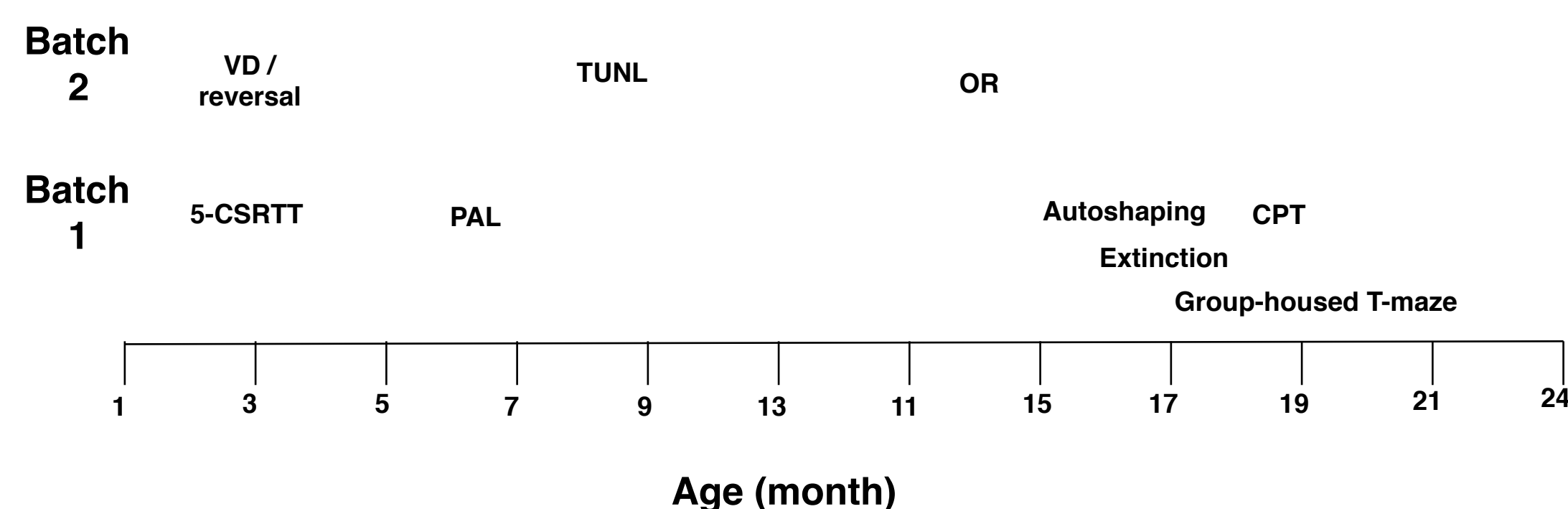
EXTINCTION LEARNING

Extinction learning involves the infralimbic cortex, striatum and the amygdala, where several 22q11.2 transgenic mice show abnormalities (Meehan et al. 2013; Ellengood et al. 2013).

OBJECT RECOGNITION

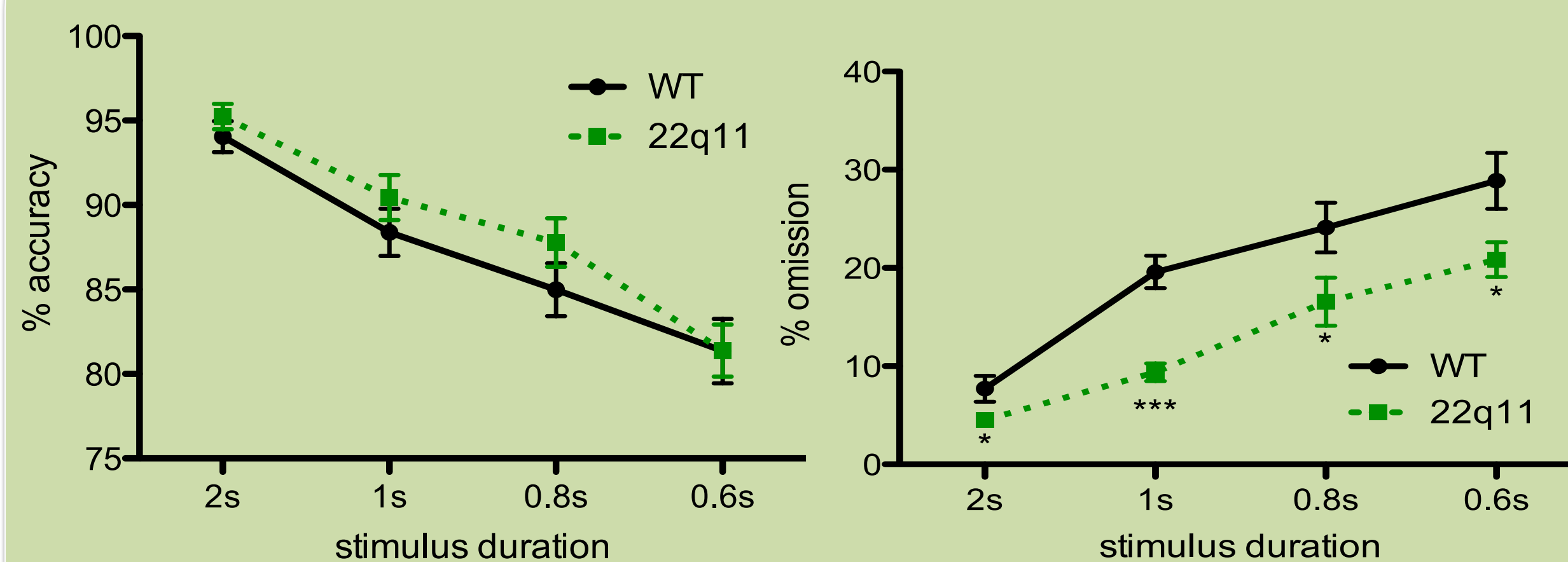
Object recognition is many impaired in transgenic and pharmacological models of schizophrenia. The task has good construct and predictive validity for the cognitive symptoms of schizophrenia.

COMPLETE TEST BATTERY



★ **Deep behavioural phenotyping of 22q11 CNV mice.** Two batches of 22q11 transgenic mice have been assessed in a battery of tasks over a 20 month period.

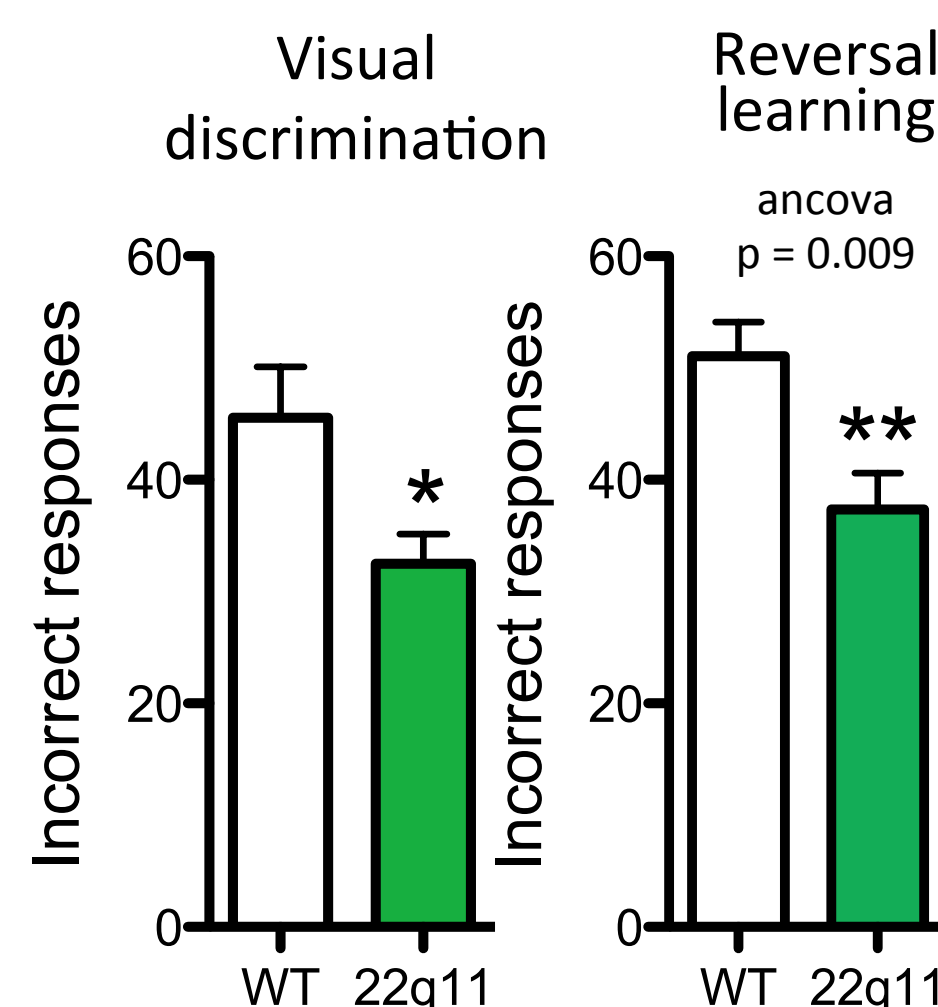
ATTENTION



★ **Improved attention.** 22q11 TGs show improved attention observed as decreased omissions at all stimulus durations. Genotype did not affect any other performance measure.

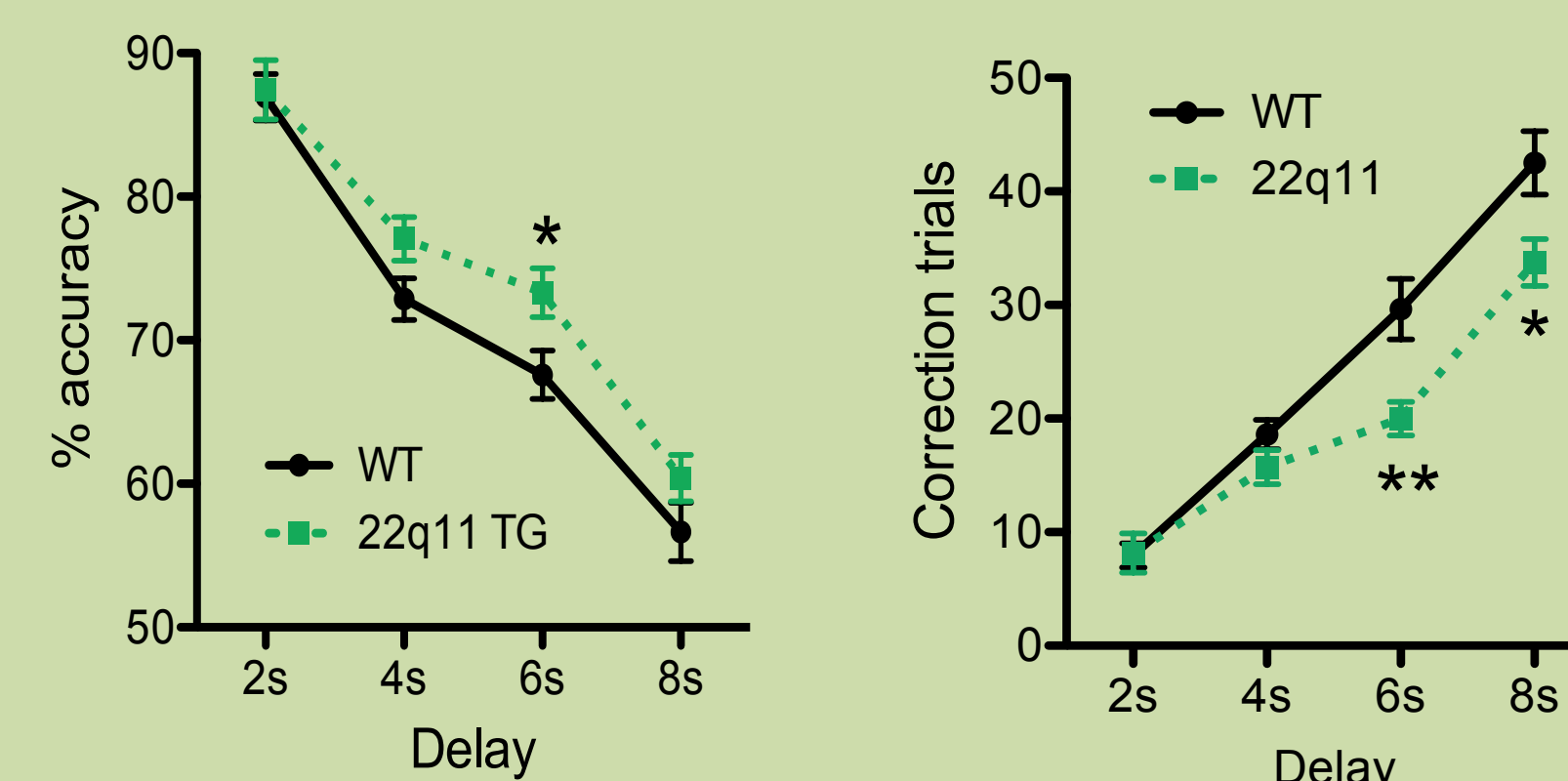
COGNITIVE FLEXIBILITY

★ **Improved discrimination learning and cognitive flexibility.** The 22q11 TG show improved visual discrimination and reversal learning. The reversal improvement remained significant when accounting for the improved discrimination performance.



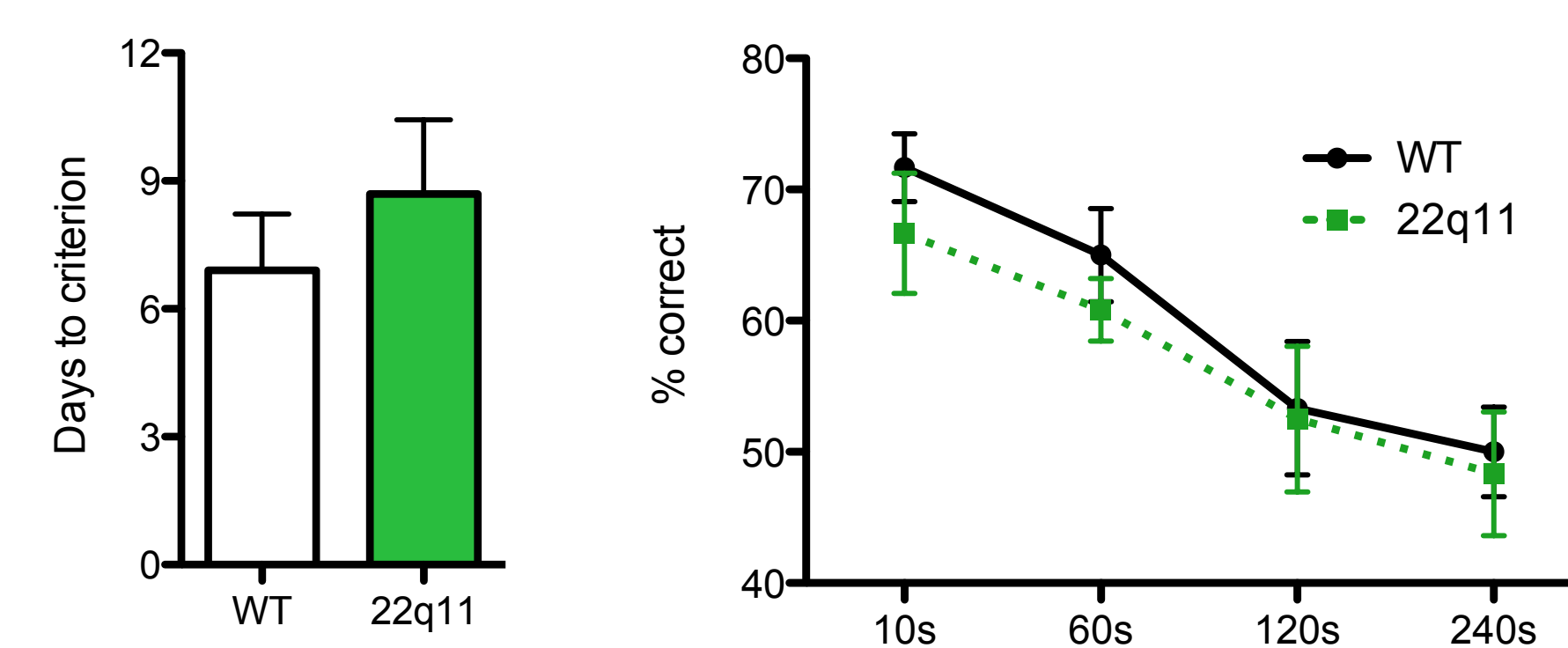
RESULTS

TOUCHSCREEN WORKING MEMORY



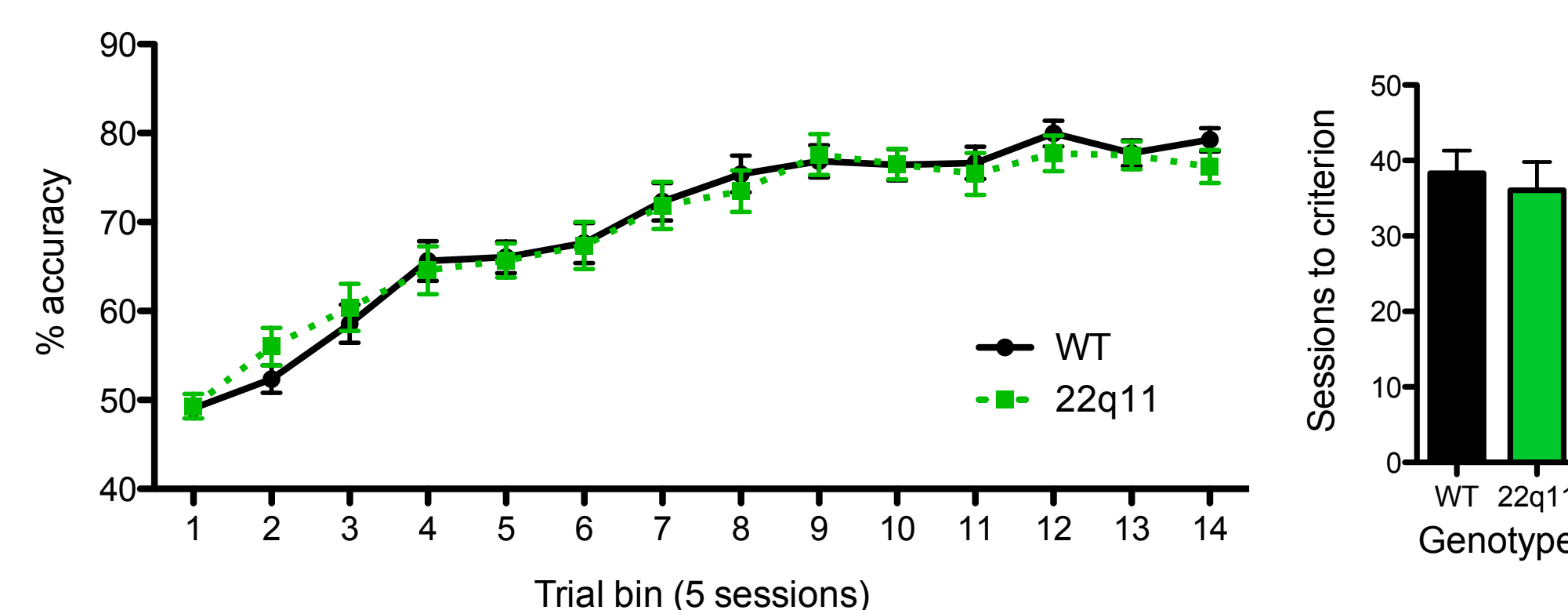
★ **Improved touchscreen working memory.** The 22q11 TGs show improved accuracy and require fewer correction trials at longer delays in a delayed non-match to location task.

T-MAZE WORKING MEMORY



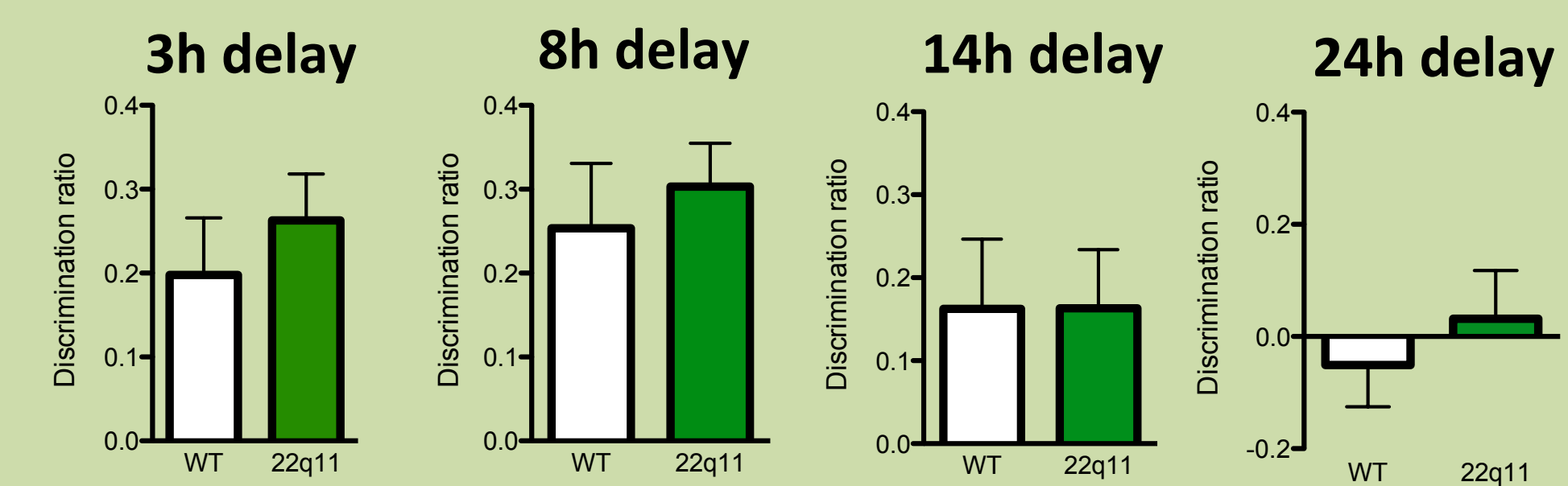
★ **No effect on T-maze delayed non-match to location.** Genotype failed to affect performance on task acquisition and performances during longer delays

VISOSPATIAL MEMORY



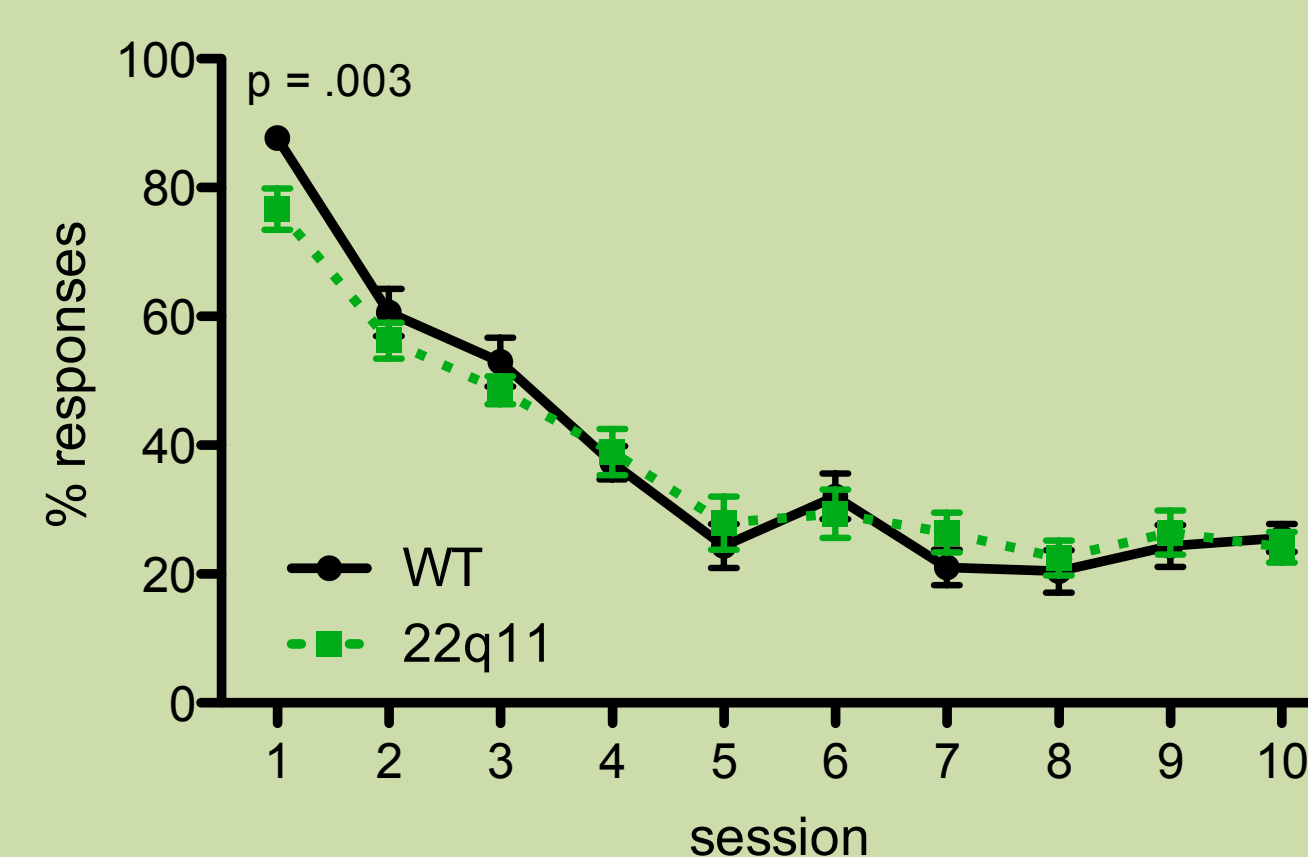
★ **No effect of genotype on object-in-place learning.** Genotype had no effect on any measure in the paired-associate learning task

RECOGNITION MEMORY



★ **No effect of genotype on object recognition.** Performance decreased equally in both genotypes across longer delays.

EXTINCTION LEARNING



★ **Trend for faster extinction learning** – with TGs omitting more responses in the very first session.

SUMMARY

Across the test battery, the 22q11 transgenic performed as well or better than their wild-type littermates. The transgenic showed improved touchscreen working memory, improved visual discrimination and reversal learning, improved attentional functioning and early extinction learning.

REFERENCES

Bearden CE et al. (2001) J Clin Exp Neuropsych 23:447–464.
Ellegood J et al. (2014) Mol Psychiatr 19:99–107.
Meehan et al. (2013) Cereb Cortex., in press.
Stark KL et al. (2008) Nat Genet 40:751–760.