DOPAMINE TRANSPORTER GENOTYPE PREDICTS IMPLICIT SEQUENCE LEARNING BUT NOT IMPLICIT SPATIAL LEARNING

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BACKGROUND INFORMATION AND PURPOSE

COGNITIVE NEUROSCIENCE increasingly incorporates genetics data to understand cognition (Green et al., 2008), though implicit learning remains understudied

IMPLICIT LEARNING is the acquisition of information about environmental regularities without intending to learn or becoming aware of what has been learned (Frensch, 1998)

A VNTR POLYMORPHISM OF THE DOPAMINE TRANSPORTER GENE (DAT1) influences dopamine transporter expression levels

- Higher density of DAT expression in the striatum (Madras et al., 2005) relative to the medial temporal lobes (Lewis et al., 2001)

THE PRESENT STUDY investigated the effects of a polymorphism of DAT1 on two forms of implicit learning: sequence learning and spatial context learning

TWO FORMS OF IMPLICIT LEARNING, sequence learning and spatial context learning, differ in (1) the regularity to be learned and (2) the underlying neural regions they engage

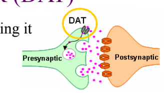
SEQUENCE LEARNING: Learning sequential dependencies among events and can be measured using the Triplets Learning Task (Howard et. al, 2008)

- Engages the medial temporal lobe network early in learning and striatal circuits later in learning (Rose et al., 2002; Schendan et al., 2003)

SPATIAL CONTEXT LEARNING: Learning regularities in spatial layouts and can be measured using the Contextual Cueing Task (Chun & Jiang, 1998)

- Engages medial temporal lobe networks (Chun & Phelps, 1999; Greene et al., 2007; Park et al., 2004; Preston & Gabrieli, 2008)

DOPAMINE TRANSPORTER (DAT)



- Responsible for clearing dopamine from synapse and recycling it back to presynaptic terminal
- Variations in DAT1 result in individual differences:

	DAT availability* (Heinz et al., 2000)	Caudate activity (Stollstorff et al., 2010)	Caudate volume (Durston et al., 2005)
9-repeat carriers (9/9 or 9/10)	Less	More	Larger
10/10 homozygotes	More	Less	Smaller

* More DAT availability means less dopamine in the synapse

PREDICTIONS

- DAT1 genotype *will* influence striatal-based learning, i.e., implicit sequence learning, particularly in the later stages of training (9-repeats > 10/10 homozygotes)
- DAT1 genotype *will not* be related to medial temporal lobe-based tasks, i.e., implicit spatial context learning

PARTICIPANTS

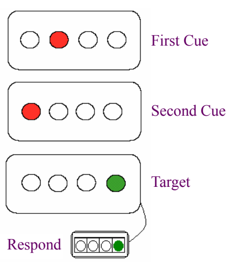
Group (n)	9-repeat carriers (15)	10/10 homozygotes (15)
Age (SD)	20.0 years (1.1)	20.1 years (1.3)
Gender	2 male, 13 female	6 male, 9 female
Education (SD)	13.9 years (1.0)	14.5 years (1.1)

- Screened for psychiatric disorders (e.g. ADHD) and drugs known to influence cognition
- No group differences (p's > .09)

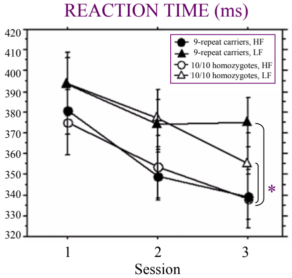
IMPLICIT SEQUENCE LEARNING

TRIPLETS LEARNING TASK

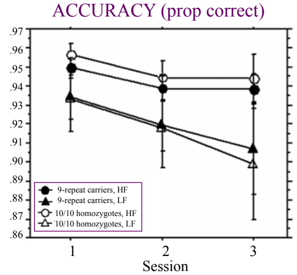
- View stimuli at 1 of 4 locations that fill in red, then green in discrete, three-event sequences or 'triplets'
- Observe red cue events and respond only to the third, green target
- 15 blocks of 50 trials, divided into 3 sessions
- A randomly chosen set of 16 triplets occurred more frequently than remaining 32 triplets (probability ratio 9:1)
- IMPLICIT SEQUENCE LEARNING: Compare triplets that occurred with High Frequency (HF) vs. Low Frequency (LF)



REACTION TIME (ms)



ACCURACY (prop correct)



ANOVA: Genotype (9-repeat carriers, 10/10 homozygotes) × Triplet Type (HP, LP) × Session (1-3)

REACTION TIME:

- Overall RT decreased across Sessions ($p < .0001$)
- Faster responding to HF vs. LF triplets ($p < .0001$)
- Separation in triplet responding increased with practice ($p = .05$)
- 9-repeat carriers show greater sequence learning, particularly with practice ($p = .03$)

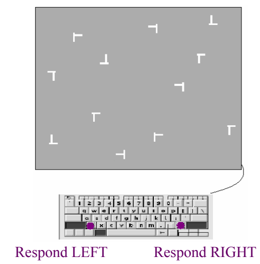
ACCURACY:

- Reached optimal level of 92% ($p = .01$)
- More accurate responses to HP vs. LP triplets ($p = .005$)
- No main effects or interactions with Genotype

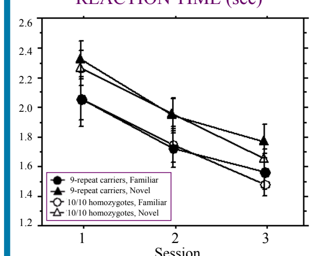
IMPLICIT SPATIAL CONTEXT LEARNING

CONTEXTUAL CUEING TASK

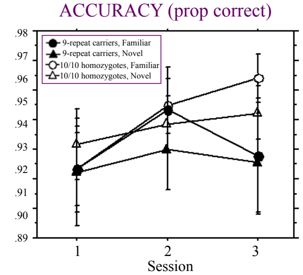
- View arrays of 11 distractors (offset L's) and 1 target (horizontal T)
- Locate the target and respond to its orientation (the tail of the T)
- 30 blocks of 12 trials, divided into 3 sessions
- A randomly chosen set of 6 arrays repeat across blocks, whereas remaining 6 arrays were novel
- Spatial layout of distractors in repeated arrays predict the target location
- IMPLICIT SPATIAL CONTEXT LEARNING: Compare arrays that are Familiar vs. Novel



REACTION TIME (sec)



ACCURACY (prop correct)



ANOVA: Genotype (9-repeat carriers, 10/10 homozygotes) × Array (Familiar, Novel) × Session (1-3)

REACTION TIME:

- Overall RT decreased across Sessions ($p < .0001$)
- Faster responding to Familiar vs. Novel arrays ($p < .0001$)
- No main effects of interactions with Genotype

Note: Subsequent ANOVA across blocks within Session 1 revealed 'quick' learning (Block X Array, $p < .05$), versus preexisting response biases to Familiar and Novel arrays

ACCURACY:

- More accurate responses to Familiar vs. Novel arrays ($p = .005$)
- No main effects or interactions with Genotype

SUMMARY AND DISCUSSION

- First study to reveal association between DAT1 genotype and implicit learning
  - Sequence Learning: 10/10 homozygotes showed less learning that 9-repeat carriers
  - Spatial Context Learning: Not influenced by DAT1 genotype
- DAT1 genotype revealed dissociation between sequence learning and spatial context learning in healthy adults, consistent with studies that find these tasks to be dependent on different brain regions (Barnes et al., in press; Howard et al.,2004; Negash et al., 2007)
  - Emphasizes significance of dopamine to sequence learning
- Our genetic makeup influences our ability to implicitly learn from our environment, consistent with previous studies (Negash et al., 2007; Keri et al., 2005; Frank et al., 2007)
- Limitations:
  - No measures of explicit knowledge, other than generalized interview after testing
  - No counterbalancing of task order

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