



VAL ALLELE HOMOZYGOTES AT BDNF VAL66MET REVEAL BETTER EARLY IMPLICIT ASSOCIATIVE LEARNING THAN MET CARRIERS

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BACKGROUND INFORMATION

PURPOSE

- To investigate the relationship between implicit associative learning and a polymorphism in the gene (rs6265) coding for Brain-Derived Neurotrophic Factor

IMPLICIT ASSOCIATIVE LEARNING (IAL):

- The acquisition of probabilistic regularities without intent or explicit knowledge
- Supported by the hippocampus and striatum at different stages of training (Poldrack & Packard, 2003)
 - Early learning recruits hippocampus whereas later learning recruits striatum (Frank et al., 2006; Poldrack et al., 2001; Schendan et al., 2003a, 2003b; Seger & Cincotta, 2006; Shohamy et al., 2009)

BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF):

- Promotes synaptic plasticity and neuronal survival (Bieder & Scharfman, 2004)
- Highest neuroanatomical expression in hippocampus (Murer et al., 2001)
- Functionally relevant single nucleotide polymorphism (SNP), val66met, controls BDNF expression, with the met allele being associated with reduced BDNF expression (Egan et al., 2003)

LOW ACTIVITY MET ALLELE IS ALSO ASSOCIATED WITH ...

- reduced hippocampal volume (Bauer et al., 2006; Chepenik et al., 2009; Frodl et al., 2007; Pezawas et al., 2004; Szesko et al., 2005)
- reduced performance in hippocampal-based tasks (Dempster et al., 2005; Egan et al., 2003; Hainri et al., 2003; Li et al., 2004)
- reduced skill acquisition/poorer early learning (Berchold et al., 2010; Limarsson et al., 1997; Mizuno et al., 2000)
- reduced processing speed/perceptual-motor processing (Miyajima et al., 2008; Raz et al., 2009)

PREDICTIONS

- Individual differences in BDNF would be associated with early, but not later IAL...
 - Val/Val homozygotes will exhibit greater learning than Met-Carriers in the first training session
- BDNF would be associated with perceptual-motor processing...
 - Val/Val homozygotes will respond faster overall than Met-Carriers

METHOD

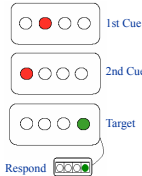
PARTICIPANTS

Group (n)	Val/Val (17)	Met-Carriers (12)
Age (SD)	20.4 years (1.1)	20.3 years (1.2)
Gender	12 females	10 females
Education (SD)	14.4 years (1.9)	14.2 years (1.1)

- Only Caucasian participants of European ancestry
- Screened for psychiatric disorders and drugs known to influence cognition
- No group differences in above (p 's > .62)

TRIPLETS LEARNING TASK

- View stimuli at 1 of 4 locations that fill in red, then green in discrete, three-event sequences or 'triplets'
- Observe two red cue events and respond only to the third, green target
- Shortened training from Howard et al. (2008)
 - 3 training sessions
 - 15 blocks of 50 trials (total)
 - Feedback (accuracy and RT) provided after each block, in attempt to guide participants to 92% accuracy
- A randomly chosen set of 16 triplets occurred more frequently than remaining 32 triplets (ratio 9:1)
- No repetitions or trials presented

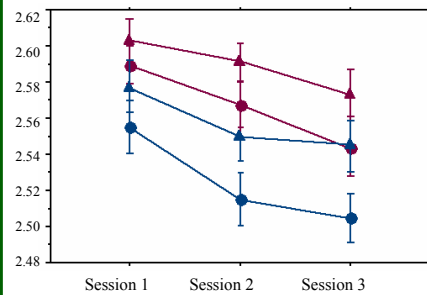


IMPLICIT SEQUENCE LEARNING

- Compare the triplets that occurred with High Probability (HP) versus Low Probability (LP)

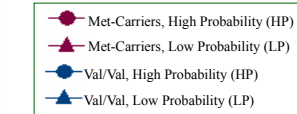
RESULTS: IMPLICIT SEQUENCE LEARNING

LOG-TRANSFORMED MEAN OF MEDIAN REACTION TIME (ms)



ACCURACY:

- Overall ~ 93%; no genotype differences
- More accurate on HP versus LP triplets ($p < .01$)
- Accuracy decreased across sessions ($p < .05$)
- Feedback guided participants to optimal accuracy

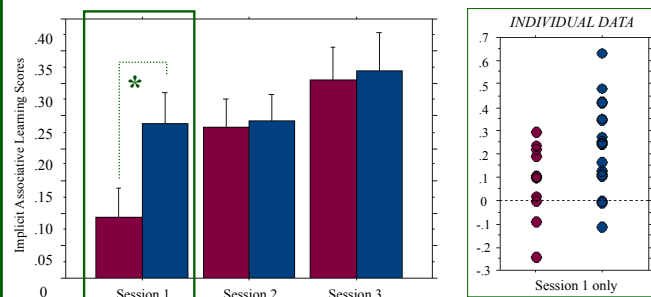


REACTION TIME:

- Val/Val faster overall than Met-Carriers ($p = .05$)
- Faster on HP versus LP triplets ($p < .001$)
- RT decreased across sessions ($p < .005$)
- Separation between triplet types increased with practice ($p < .05$)
- Val/Val show marginally greater sequence learning than Met-Carriers ($p = .07$)

RESULTS: IMPLICIT ASSOCIATIVE LEARNING (IAL) SCORES

- IAL is greater than 0 in Val/Val homozygotes in all 3 sessions (p 's < .05)
- IAL is greater than 0 in Met-Carriers in sessions 2 and 3 only (p 's < .05)
- IAL greater in Val/Val than Met-Carriers in session 1 only ($p < .05$)



CALCULATING IMPLICIT ASSOCIATIVE LEARNING SCORES

- Group difference in overall RT complicates genotype comparisons of the HP versus LP triplets RTs (Curran, 1997)
- So, for each participant on each session, we determined the median RT for each unique triplet
- These median reaction times were then correlated with the number of times that each individual triplet actually occurred (i.e., each triplet's frequency of occurrence)
- Each correlation was multiplied by -1, for ease of interpretation, and converted to z-scores using Fisher's transformation
- Higher scores reflect greater associative learning (i.e. triplets occurring with HP would be responded to more quickly) whereas lower scores (e.g., 0) reflect no associative learning

SUMMARY AND DISCUSSION

RESULTS SUMMARY

- As predicted, Met-Carriers:
 - Showed less IAL than Val/Val early, but not later, in training
 - Responded more slowly overall

BDNF AND EARLY IMPLICIT ASSOCIATIVE LEARNING (IAL)

- Our genetic makeup influences our ability to implicitly learn from our environment, consistent with previous work (Frank et al., 2007; Keri et al., 2005; Negash et al., 2007; Simon et al., 2010)
- Early and late IAL can be dissociated by underlying neural mechanisms (Poldrack & Packard, 2003)
- Some individual differences in early IAL are related to BDNF genotype
 - Consistent with reports that BDNF availability is related to hippocampal-dependent skill acquisition, such that higher levels of BDNF protein correspond to better initial learning (Berchold et al., 2010; Limarsson et al., 1997; McHughen et al., 2009; Mizuno et al., 2000)
- BDNF expression may alter neuronal processes that influence hippocampal-based skill acquisition
 - Consistent with reports that BDNF has rapid and short-term effects on synaptic plasticity necessary for memory formation (Bokinshtein et al., 2008; Lu, 2003; Tyler et al., 2002)

BDNF AND PROCESSING SPEED

- Variations in BDNF expression may influence general processing resources, including motor system functioning (McHughen et al., 2009)
 - Met-Carriers have been found to have slower finger tapping rates (Echeverria et al., 2005; McHughen et al., 2009, Exp. 2)
 - Met-Carriers are reported to have reduced processing speed and perceptual-motor processing (Miyajima et al., 2008; Raz et al., 2009)

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