Reward Processing in Social Competitive Task in Subjects with Familial History of Alcoholism

Gregory A Book[1], Andre D Thomas[1], Matthew R Johnson[4], Jennifer L Hylton[1], Melissa M Andrews[1], Michal Assaf[1,2], Godfrey D Pearlson[1,2,3]

[1]Olin Neuropsychiatry Research Center, Institute of Living at Hartford Hospital, Hartford, CT; [2]Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT; [3]Dept. of Psychiatry, Johns Hopkins University, Baltimore, MD; [4]Interdepartmental Neuroscience Program, Yale University, New Haven, CT

Background

Healthy subjects demonstrate activation in the "reward circuit", especially in the ventral striatum (nucleus accumbens, NAcc) during reward anticipation, during performance of the Monetary Incentive Delay Task (Hommer et al, 2003). Alcoholic subjects, and possibly those with a family history of alcoholism, fail to show this NAcc activation, However, the relationship of this finding to brain activation during reward processing of socially relevant, rather than monetary information is unclear. We investigated the brain circuits involved in processing of reward anticipation in healthy participants with and without a positive family history of alcoholism using a social, competitive decision-making task (Kahn et al, 2002).

Hypothesis

We hypothesized that areas of the reward circuit will show abnormal activations in healthy individuals with a family history of alcohol abuse compared to individuals without such history, while engaging in reward anticipation during a social, competitive game

Decision Making Task (Domino)
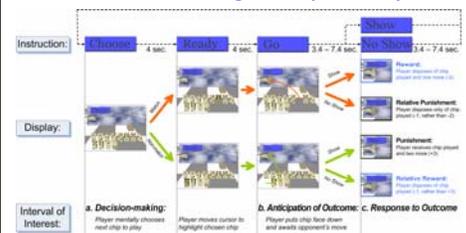
Flow of the Domino game. Conditions of interest for this analysis are activations in the Anticipation of Outcome Interval resulting from picking a matching chip (PM, i.e. anticipating possible reward) and picking a non-matching chip (PNM, anticipating possible punishment).

Methods

Thirty five healthy subjects, 16 with a positive family history of alcohol abuse (mean 35y ±15y; 12F), 19 with a negative family history (mean 39y ±14y; 13F) participated. Subjects were tested using functional MRI while playing a goal-directed, competitive Domino game against what they believed was a human opponent.

Winning involved having to bluff the opponent on occasion (i.e. playing a non-matching chip); which would result in a risk of being caught and punished. Players were rewarded if they were "caught" while playing fairly (i.e. a matching chip). We analyzed a predefined interval during the game, the Anticipation to Outcome interval, during which participants had already chosen to bluff or play fairly, but were not yet aware of their opponent's response; thus they did not know if they were going to be punished or rewarded.

fMRI data were realigned using INrealign, normalized to the standard EPI template, and smoothed at 9mm. Statistics were created using the general linear model (GLM) in SPM2, generating first level (subject) and second level (group comparison) statistics.

Behavioral Results

No significant differences were found between groups for the percentage of games won. FHP won 20% of games started, and FHN won 25% (t=1.42, p>0.10).
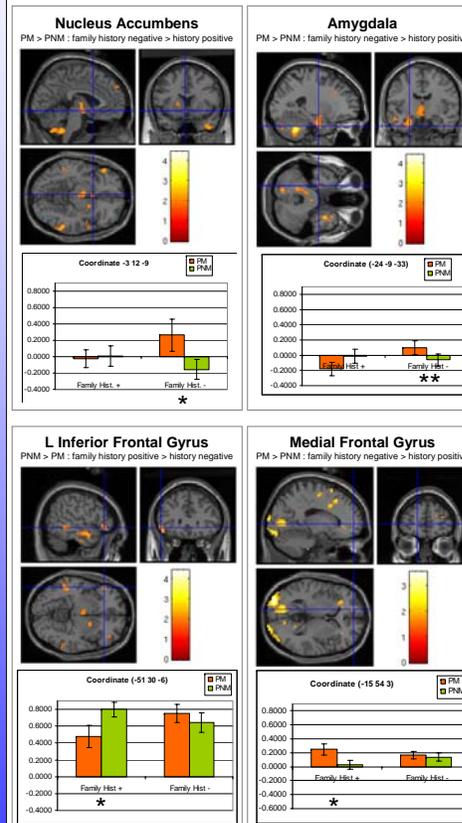
References

• Kahn I, Yeshurun Y, Rotshtein P, Fried I, Ben-Bashat D, Hendler T (2002) The role of the amygdala in signaling prospective outcome of choice. Neuron 33:983-994.
• Hommer, D. W., Knutson, B., Fong, G. W., Bennett, S., Adams, C. M., & Varnera, J. L. (2003). Amygdalar recruitment during anticipation of monetary rewards: an event-related fMRI study. Annals of the New York Academy of Sciences, 985, 476-478.

Acknowledgements

Results

Nucleus Accumbens
PM > PNM : family history negative > history positive
Coordinate -3 12 -9

Amygdala
PM > PNM : family history negative > history positive
Coordinate (-24 -9 -33)

L Inferior Frontal Gyrus
PNM > PM : family history positive > history negative
Coordinate (-51 30 -6)

Medial Frontal Gyrus
PM > PNM : family history negative > history positive
Coordinate (-15 54 3)

* Indicates a significant difference between PM and PNM (p<0.05)
** Indicates a trend between PM and PNM (p<0.06)

Abbreviations
FHP – Family history positive
FHN – Family history negative
PM – Pick Match (possible reward)
PNM – Pick Non-Match (possible punishment)

fMRI Results

Several areas in the reward circuit showed abnormal activation between the FHP and FHN subjects, including the NAcc and amygdala.

▪ The **NAcc**, with coordinate (-3,12,-9) showed a group difference between FHP and FHN (t=1.86, p<0.05). The FHN group showed significantly greater activation for PM than PNM conditions (t=2.23,p=0.039). No significant differences were shown between PM and PNM for the FHP group.

▪ The **amygdala**, with coordinate (-24, -9, -33) showed significant group differences (t=2.44, p<0.05). No significant differences were found between the PM and PNM conditions for either group, though FHN showed a trend for PM being greater than PNM, with p=0.06.

▪ The **left inferior frontal gyrus**, with coordinate (-51,30,-6) showed a significant group difference (t=2.53,p<0.05). Activation for the PNM condition was significantly greater than PM for the FHP group (t=2.40,p=0.03).

▪ The **medial frontal gyrus**, with coordinate (-15,54,3) showed a group difference (t=1.92, p<0.05). Activation for the PM condition was significantly greater than PNM for the FHP group (t=2.98,p=0.009).

Conclusions

Though otherwise healthy, individuals with a family history of alcohol abuse showed abnormal activations in the reward circuit, including the NAcc, when compared to family history negative individuals during a social, competitive task. These results suggest that at least some family history positive individuals may carry a genetic component of alcoholism, which influence their processing of socially relevant reward stimuli and might also be in the basis of alcohol abuse in their family members. Therefore, activation during the Domino task might be used as a biomarker to help identifying the risk gene/s for alcoholism.