Association between opioid receptor availability and anxiety in healthy controls but not in substance dependence

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Introduction

- Positron Emission Tomography (PET) can be used to image accurately opioid receptor availability in vivo.1,2,3
- Using [11C]diprenorphine PET, opioid receptor availability has been reported to be elevated in early abstinence from dependent opioid use when compared with normal controls.1
- Elevated opioid receptor availability in early abstinence from dependent alcohol and cocaine use compared with normal controls has been reported using [11C]carfentanil PET.4,5
- It is unclear whether these findings are a cause or consequence of substance dependence since evidence linking amount and duration of substance use with opioid receptor availability is limited.6
- Naltrexone, an opioid receptor antagonist, has been reported to improve abstinence rates after detoxification from drug and alcohol dependency, further adding weight to the opioid receptor system being important in the abstinence phase of the addiction cycle.
- Genetic variants for the μ, δ and κ opioid receptors OPRD1 and OPRK1 have been shown to be risk factors for drug and alcohol dependency, suggesting that variation in opioid receptor genotype and therefore function could be important in individuals developing drug and alcohol dependencies.
- As a longitudinal study involving PET at an early age is not currently feasible, to examine whether high opioid receptor availability is associated with risk of subsequent drug and alcohol dependencies, we focus here on state and trait anxiety levels measurable in adulthood to investigate their relation with opioid receptor availability as measured by [11C]diprenorphine PET in dependent and non-dependent populations.

Methods

- We recruited 10 opioid and 10 alcohol dependent subjects and 13 healthy controls. [fig 1].
- All subjects underwent one [11C]diprenorphine PET scan following standard protocols.
- An analysis of ligand volume of distribution (VI) globally and in 21 a priori regions was produced using an automated protocol.
- Anxiety levels were measured with Spielberger's State (SSAI) and Trait (STAI) Anxiety Inventories.
- Difference in means were compared with a one-way ANOVA, correlations were performed using SPSS and reported as Spearman's correlation co-efficient.

<table>
<thead>
<tr>
<th>Opioid dependent subjects (n=10)</th>
<th>Alcohol dependent subjects (n=10)</th>
<th>Control subjects (n=13)</th>
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</thead>
<tbody>
<tr>
<td>Mean age (years ± SD)</td>
<td>31.7 ±6.3</td>
<td>43.8 ±10.5</td>
</tr>
<tr>
<td>Male : Female</td>
<td>8 : 2</td>
<td>10 : 0</td>
</tr>
<tr>
<td>SSAI score (±SD)</td>
<td>43.7 ±6.8</td>
<td>34.0 ±9.7</td>
</tr>
<tr>
<td>STAI score (±SD)</td>
<td>44.5 ±11.5</td>
<td>41.8 ±13.3</td>
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</tbody>
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**Figure 1.** Demographic data and state and trait anxiety scores.

Results

- There was a significant difference in the ages between the groups with the opioid dependent subjects being significantly younger (ANOVA p=0.05).
- There were significant differences between the groups on the SSAI (ANOVA p=0.007) but no difference on the STAI (p=0.22) [fig 1].
- No significant correlation was found between global VD and SSAI across all 31 subjects (p=0.230, p=0.215), or when controls (p=0.673, p=0.130), alcohol dependent subjects (p=0.064, p=0.861), and opioid dependent subjects (p=0.142, p=0.696) were analysed separately.
- However there was a significant positive correlation between global VD and STAI across all 31 subjects (p=0.422, p=0.014).
- This correlation was also evident in the control subjects (p=0.655, p=0.015) [fig 2], but not when alcohol dependent subjects (p=0.226, p=0.529) and opioid dependent subjects (p=0.044, p=0.904) were analysed separately [fig 3].
- On a regional analysis, STAI scores showed a significant positive correlation with VD in all the 21 a priori brain regions studied in the control subjects (n=13).
- There was no correlation between regional VD and trait anxiety in either of the dependent groups.
- There were no significant correlations between state anxiety and VD regionally across all subjects or when the groups were analysed separately.

Conclusions

- We have found for the first time a significant correlation between opioid receptor availability and trait anxiety in normal controls.
- Interestingly there is no such correlation in both the substance dependent populations studied.
- Furthermore despite a significant difference in state anxiety between the groups there was no correlation between state anxiety and opioid receptor availability.
- We have previously shown an association between the neuroticism personality trait and opioid receptor availability in alcohol dependent subjects and normal controls.6
- These data further pinpoint the biological basis for an association between anxiety and substance dependence.
- It is possible that trait or underlying propensity to anxiety is a risk factor for substance dependence and is mediated by higher opioid receptor levels.
- Anxiety disorders are commonly linked with other receptor systems, particularly GABA. However, this evidence suggests that the opioid receptor system should not be overlooked.
- Furthermore, if simple measures of trait anxiety correlate reliably with opioid receptor availability, these measures could be used as a marker for people who have high opioid receptor availability who may be at greatest risk for developing substance dependence.

Acknowledgements

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References