Chronic depersonalization following illicit drug use: a controlled analysis of 40 cases

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ABSTRACT

Aims To examine demographic and clinical features of a group of patients reporting chronic depersonalization (DP) following illicit drug use, and to assess whether depersonalization arising in these circumstances constitutes a distinct clinical syndrome.
Design Case–control comparison using self-reports, standardized questionnaires and clinical assessments in a specialized clinic.
Setting A tertiary referral depersonalization clinic and research unit affiliated to a psychiatric hospital and research centre.
Participants A total of 164 individuals with chronic DP symptoms who had been in contact with the clinic. Forty of these individuals related the onset of symptoms to an episode of illicit drug use.
Measurements A wide range of demographic and clinical variables measured using questionnaires and standardized rating scales.
Findings The drug-induced DP group were significantly younger and had a preponderance of males compared to the non-drug group. Certain clinical and phenomenological differences were found between these groups, but in general the groups are strikingly similar. This is reinforced by the fact that when the drug-induced group was compared with an age and sex-matched subset of the non-drug group, differences between groups largely disappeared.
Conclusions Drug-induced DP does not appear to represent a distinct clinical syndrome. The neurocognitive mechanisms of the genesis and maintenance of DP are likely to be similar across clinical groups, regardless of precipitants.

KEYWORDS Cannabis, depersonalization, derealization.

INTRODUCTION

Depersonalization (DP) remains a common (Brauer et al. 1970) but little-studied phenomenon, although recent work has aimed to illuminate the symptomatology (Siméon et al. 1997) and underlying neurobiology (Siméon et al. 2000; Phillips et al. 2001). Persistent DP may occur as a primary disorder or in a range of neuropsychiatric contexts (e.g. schizophrenia, temporal lobe epilepsy, major depressive disorder). It occurs commonly with derealization (DR), the DP–DR symptom complex being characterized by a feeling of detachment from one’s surroundings (DR), and one’s own emotions, sensory perceptions and sense of self (DP), such that both self and environment take on a disturbing air of unreality. Other symptoms that may occur include de-affectualization (a profound numbing of emotion, sometimes so marked that sufferers complain of experiencing no emotions at all), desomatization (a sense of disconnection from one’s body), and perceptual anomalies such as a two-dimensional appearance of the surroundings, or a blunting of sensation across modalities (see Mayer-Gross (1935) for an array of striking self-reports).

In health, transient DP–DR occurs commonly in fatigue, in the face of extreme danger, and during or following intoxication with alcohol and/or drugs, and some
sufferers from chronic persistent DP attribute the onset of their symptoms to a specific episode of illicit drug use. Small case-series of apparently drug-induced chronic DP have been reported (Szymanski 1981; Keshaven & Lishman 1986; Moran 1986), but this study represents the first attempt to compile sufficient information to describe the course and phenomenology of DP–DR following drug use. The purpose of this study was to examine the characteristics and symptomatology of this DP subgroup, and compare the findings with those in DP–DR sufferers with no history of drug abuse.

**METHOD**

Cases were drawn from the database of referrals to the Depersonalization Research Unit, Maudsley Hospital, London. This database contains clinical and demographic data on individuals whose primary psychiatric symptoms are those of chronic DP–DR (Baker et al. 2003). Questions regarding drug use were asked as items on a standard questionnaire, which all patients completed as part of the process of referral to the Unit. Patients are asked whether their symptoms first occurred in the context of drug use and if so, to identify the drug(s) involved, and whether alcohol was used concurrently. Further items probe for a history of ongoing drug use, and the relationship of symptoms to such use. More generally, the questionnaires probe the course and nature of the symptoms, subjects' personal and clinical histories (including history of other symptoms, such as anxiety, panic attacks, hallucinations, migraine and tinnitus) and the relationship, if any, of DP–DR to other symptoms (questionnaires available on request).

Frequency of symptoms was rated on a scale of 1 (‘rarely’) to 7 (‘all the time’). All subjects completed a range of other standard rating scales and symptom inventories. These were the Dissociative Experiences Scale (DES) (Bernstein & Putnam 1986), in which subjects mark a visual analogue scale to indicate the frequency of specific phenomena (some items relate to DP–DR, but the scale covers a range of experiences, including pseudohallucinations, *jannais vu* and memory lapses). This allows calculation of both a total score and a score for specific DP–DR items, as in Simeon et al. 1998), the Beck Depression and Anxiety Inventories (BDI, BAI) (Beck et al. 1961; Beck & Steer 1990), the Spielberger State and Trait Anxiety Inventories (SSAI, STAI) (Spielberger 1983) and the Cambridge Depersonalization Trait (CDTS) (Sierra & Berrios 2000) and State (CDSS) Scales (copies available on request). The 29-item CDTS asks subjects to score both the frequency and the duration of phenomena relevant to DP–DR; these are then combined to generate a total score for each item. The CDSS is a 22-item state scale derived from the CDTS. Respondents are asked to rate the current (i.e. at that moment) intensity of particular symptoms on a visual analogue scale, from 0% to 100%. Clinical data were used to derive ratings for items of the Present State Examination (PSE) which relate to DP and DR (Wing et al. 1974). Information gathered enabled us to summarize the clinical and demographic characteristics of the drug and non-drug DP groups.

Initial comparisons were made between the total drug group (n = 40) and the total non-drug group (n = 124). Of the 40 drug-induced cases, 25 (62.5%) had received a clinical assessment by a psychiatrist attached to the Depersonalization Research Clinic. Of the 124 non-drug cases, 76 (61.3%) had received such an assessment. The remaining subjects completed all the questionnaires and rating scales listed above, and were evaluated on the basis of data thus obtained. No significant demographic or clinical differences were found between subjects who had been assessed in the clinic and those who had not. All subjects gave written informed consent regarding participation in the study.

Further comparisons were then carried out between the 40 drug-induced cases and an age- and sex-matched sample of 40 cases from the non-drug group. This was undertaken to examine the possibility that younger case groups with a preponderance of males (as in our drug-induced group) may differ from other DP cases on certain measures, regardless of history of drug abuse.

Of the 40 drug-induced cases, 20 attributed the onset of their symptoms to the use of cannabis alone. After results from the entire drug-induced group had been analysed, further analysis was performed on data from the cannabis subgroup.

**RESULTS**

Forty subjects (30 males, 10 females, aged 16–51 years, mean 29.9, SD = 8.9) attributed the onset of their symptoms to an episode of illicit drug use, with DP symptoms beginning either during the period of intoxication or within 72 hours of ingesting the drug. Twenty attributed the onset of their symptoms to cannabis, four to MDMA (ecstasy), two to LSD and one to ketamine. The remaining 13 attributed symptom onset to an episode involving use of multiple drugs, with various combinations (all involving at least one of cannabis, MDMA and LSD) described, e.g. ‘cocaíne and cannabis’, ‘cocaíne, amphetamines, ecstasy’. Twenty-seven of these 40 subjects stated that the episode was their first experience of the drug(s), with only one subject describing previous exposure.
Information on previous drug experience was not available for the remaining 12 subjects.

Comparisons between drug (n = 40) and non-drug (n = 124) groups

Initial comparisons were made between the 40 cases above and the 124 non-drug-induced cases (64 males, 60 females). The mean age was significantly greater in the non-drug group (range 18–74 years, mean 37.9, SD = 11.9) (unpaired t-test, two-tailed, t = −3.86, df = 152, P < 0.001). Using the observed gender distribution in the non-drug group as expected values, a χ² test showed a significant difference between groups (χ² = 8.76, df = 1, P = 0.003).

Table 1 shows the key comparisons in symptom scales between the drug and non-drug groups. On the CDSS, CDTS, DES, BDI, BAI, SSAI, STAI and the relevant items from the PSE, there were no significant differences between total scores for the drug and non-drug groups. However, the drug group reported significantly shorter duration of DP–DR symptoms in years, but significantly higher frequency of these symptoms (when asked to rank symptom frequency on a scale of 1–7). In addition, the following were rated as more intense by the drug group: CDSS item 2 (`Things around me are looking flat or lifeless'), item 14 (`Objects look smaller or further away') and item 22 (`I am having/still having the same strange feeling as when I began filling in this questionnaire'), and CDTS item 2 (`What I see looks flat or lifeless') and item 23 (`Sometimes I have the feeling of being outside my body'). The drug group had a significantly lower score on CDTS item 28 (`I seem to have lost some bodily sensations, such as thirst or hunger'). These differences were significant at the P < 0.05 but not the P < 0.01 levels. There were no significant differences on any other individual scale items.

Significantly more members of the drug group reported using alcohol immediately prior to symptom onset: 16 (76.2%) versus 12 (9.7%) of the non-drug group (P < 0.001). Very few subjects had ever received treatment for alcohol or drug abuse (five members of the non-drug group and two of the drug group). Only one member of the drug group and two members of the non-drug group reported ongoing drug use (cannabis in all cases).

In response to the questionnaire item regarding history of anxiety and/or panic attacks, 36 (90%) of the drug group reported such a history, compared with 36 (29%) of the non-drug group (P = 0.001), although this difference was not reflected in scores on anxiety inventories.

Within the drug group, in a few cases (n = 4) the initial history was of occasional episodic depersonalization, invariably becoming more frequent over time, often becoming continual within 2–3 years of onset. In others (n = 14) the history was of sudden onset of unremitting DP–DR, either during or in the aftermath of drug intoxication. The remainder described speed of symptom onset on a continuum between these extremes.

### Table 1

<table>
<thead>
<tr>
<th>Drug group (n = 40)</th>
<th>Non-drug group</th>
<th>t (a)</th>
<th>df (a)</th>
<th>p (a)</th>
<th>ASM non-drug group (n = 40)</th>
<th>t (b)</th>
<th>df (b)</th>
<th>P (b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (years)</td>
<td>8.9 (8.6)</td>
<td>1.47 (1.30)</td>
<td>−3.32</td>
<td>0.002**</td>
<td>11.3 (8.9)</td>
<td>1.24</td>
<td>77.9</td>
<td>0.217</td>
</tr>
<tr>
<td>Frequency</td>
<td>6.9 (0.4)</td>
<td>6.0 (2.0)</td>
<td>4.11</td>
<td>0.047*</td>
<td>6.4 (1.6)</td>
<td>1.65</td>
<td>40.9</td>
<td>0.107</td>
</tr>
<tr>
<td>CDSS item 2</td>
<td>(418.0)</td>
<td>507 (37.6)</td>
<td>2.28</td>
<td>0.047*</td>
<td>76.9 (32.9)</td>
<td>0.14</td>
<td>73.3</td>
<td>0.886</td>
</tr>
<tr>
<td>CDSS item 14</td>
<td>39.1 (36.8)</td>
<td>24.6 (3.7)</td>
<td>2.16</td>
<td>0.047*</td>
<td>5.5 (3.1)</td>
<td>0.72</td>
<td>73.4</td>
<td>0.089</td>
</tr>
<tr>
<td>CDSS item 18</td>
<td>25.0 (18.2)</td>
<td>23.9 (18.8)</td>
<td>0.33</td>
<td>0.744</td>
<td>24.6 (11.4)</td>
<td>0.86</td>
<td>74.0</td>
<td>0.393</td>
</tr>
<tr>
<td>CDTS item 28</td>
<td>22.3 (11.5)</td>
<td>21.3 (12.3)</td>
<td>0.35</td>
<td>0.725</td>
<td>24.2 (10.7)</td>
<td>0.76</td>
<td>76.9</td>
<td>0.448</td>
</tr>
<tr>
<td>BDI</td>
<td>54.7 (13.7)</td>
<td>54.8 (13.6)</td>
<td>0.69</td>
<td>0.493</td>
<td>55.2 (15.3)</td>
<td>0.58</td>
<td>62.4</td>
<td>0.566</td>
</tr>
</tbody>
</table>

BDI, BAI, SSAI, STAI scores are total scores for these scales. DES scores are mean score for the 28 DES items. DES DP/DR is the score for the depersonalization/derealization taxon of the DES (total of DES items 7, 11, 12, 13, 27, 28). Mean scores are shown, standard deviations in brackets. Comparisons marked (a) are between the drug group and the total non-drug group, those marked (b) are between the drug group and an age- and sex-matched (ASM) subset of the non-drug group (see text for details). Comparisons marked with * are significant at the P < 0.05 level, those marked ** are significant at the P < 0.01 level.
Comparisons between drug group and age and sex-matched sample of non-drug group (n = 40)

As the groups compared above differed significantly in age and gender weighting, 40 subjects (30 male, 10 female, aged 18–51 years, mean 30.38) were selected from the non-drug group to generate a sample matched as closely as possible to the drug group for age and gender composition. Comparisons were then made between the drug group and this age and sex-matched sample (Table 1). The trend for the drug group to report shorter duration but increased frequency of symptoms was no longer significant, and similar non-significant findings were obtained for the CDSS and CDST items detailed above, except for CDST item 28, which still showed a significantly lower mean score in the drug-induced group. The finding that alcohol use immediately preceding symptom onset was significantly more common in the drug group was preserved.

Comparisons between cannabis group (n = 20), and age and sex-matched sample of non-drug group (n = 40)

For these comparisons, the 40 non-drug cases above were compared with the 20 patients (13 male, seven female, mean age 29.4 years) who attributed the onset of their symptoms to cannabis use alone. The groups did not differ significantly in age or gender composition. Across all questionnaires and rating scales, the only significant differences between groups were found for the following items: the experience of seeing flashes of light was significantly more common in the cannabis group (13 of 18 who answered this question) than the non-drug group (11 of 35 who answered) ($\chi^2 = 13.9, \text{df} = 1, P < 0.001$). The mean score on CDST item 28 was again significantly higher in the non-drug group (mean in cannabis group 2.1, SD 3.46. Mean in non-drug group 4.32, SD 3.81, $t = 2.17, \text{df} = 56, P = 0.034$).

**DISCUSSION**

We identified 40 cases where subjects attributed the onset of DP–DR to illicit drug use. It should be acknowledged that the initial purpose of data collection was to compile a range of clinical and demographic information relating to DP–DR rather than to study drug use as an individual topic, and this is reflected in certain limitations, e.g. full data on previous drug experience was not available for all subjects. Conversely, the range of data collected allow us to report that findings regarding course and onset of DP in the drug group are similar to those of a study (Simeon et al. 1997) of depersonalization disorder not related specifically to drug use, where between one-third and one-half of the patients reported abrupt onset of symptoms.

The most striking difference between drug and non-drug groups was that the former group was significantly younger, with a preponderance of males. The question of a possible gender bias for DP–DR was raised in the study cited above, where an approximately 2:1 female: male ratio was described. This is in contrast to the 1:1 ratio described in DSM-IV—a ratio mirrored by the non-drug group in the present study. However, the drug-induced group showed a male: female ratio of 3:1. This may, in part, reflect higher rates of illicit drug use among men (Farrell & Strang 1994), but it may also reflect a specific vulnerability of males to develop DP–DR symptoms following drug use.

Certain variables of perceptual disturbance (micropsia and macropsia, somatosensory anomalies), and also the feeling of being outside one’s body, were rated as either more common or more intense by the drug group, and the experience of seeing flashes of light was reported more commonly in the cannabis group than the non-drug group. This could be interpreted as evidence that disturbances of the sensorium in DP–DR are more pronounced when symptoms follow drug use. Overall, however, the data do not support this idea: first, in view of the multiple comparisons used in this study, $P < 0.01$ represents a more realistic probability threshold than $P < 0.05$, and only one of these differences (flashes of light) was significant at this level. Secondly, these differences largely disappeared after age and sex-matching, suggesting that they owe more to age and gender than to any history of drug use. Self-reported histories of anxiety and/or panic were significantly higher in the drug group than the total non-drug group, but again this difference was not found after sample matching, nor was it reflected by scores on anxiety inventories. This suggests that younger male DP–DR patients will tend to report more rapid symptom progression, and higher rates of anxiety and/or panic, than other patient groups. Items relating to a two-dimensional appearance of the surroundings were rated significantly higher by the drug group compared with the total non-drug group, but these same items also showed a significant negative correlation with age across the whole database, i.e. younger patients tend to rate these items higher, regardless of drug use (for CDTS item 2, Pearson coefficient = -0.158, $P = 0.047$. For CDSS item 2, Pearson coefficient = -0.157, $P = 0.049$).

That the drug group were more likely to report use of alcohol immediately preceding onset of DP–DR is unsurprising: all these subjects were, by definition, in a situation involving drug use just prior to the onset of symptoms, and it is likely that alcohol would also have been available. The question of whether alcohol contributed to the symptoms cannot be resolved from these data, although none of these 40 subjects attributed their symptoms to alcohol, but rather to the other drug(s) they had...
ingested. It may be that previous familiarity with the effects of alcohol led to a subjective certainty that it did not induce the DP.

It is not obvious why the non-drug group should have scored significantly higher on CDST item 28, an item relating to the loss of hunger or thirst (a finding that survived the age and sex-matching process). This could reflect affective symptoms, although this is not supported by significant differences on any other items or scales (such as the BDI). This is the only measure where the non-drug group scored higher than the drug group, so could be a chance finding.

The overall picture is that the drug and non-drug groups are remarkably similar on a wide range of measures when confounds such as age and gender are taken into account, suggesting that the neurocognitive mechanisms underlying the development of DP–DR may also be similar across the groups. Psychological (Sedman 1970) and biological (Sierra & Berrios 1998) models conceive of DP–DR as a maladaptive defence against overwhelming anxiety. Emotional responses are ‘shut down’, leading to de-affectualisation with associated loss of emotional tone in the experience of oneself (depersonalization, desomatization) and one’s surroundings (derealization). This unpleasant and unfamiliar feeling may then generate further anxiety, setting up a vicious cycle. Support for this view comes from a study in which healthy individuals reported DP–DR in response to danger (Noyes & Kletti 1977) and from psychophysiological data (Sierra & Berrios 1998) to be due to prefrontal regions inhibiting limbic areas, with reciprocal actions of dorsolateral prefrontal and anterior cingulate cortex (Phillips et al. 2001). Anterior cingulate cortex is thought to have a key role in emotion regulation (Drevets 2000), and a PET study of response to tetrahydrocannabinol (THC) found a significant correlation between anterior cingulate activation and THC-induced DP (Mathew et al. 1999). The idea that the anterior cingulate may have a role in the genesis and maintenance of DP–DR thus has some empirical support, although current data are far from conclusive. Future work will involve functional neuroimaging studies to further examine the neural correlates of both idiopathic and ketamine-induced depersonalization, aiming in particular to clarify the nature of cortical-limbic interactions in this fascinating but poorly understood condition.

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