The subjective experience of taking antipsychotic medication: a content analysis of Internet data

Moncrieff J, Cohen D, Mason JP. The subjective experience of taking antipsychotic medication: a content analysis of Internet data.

Objective: We explored the subjective effects associated with olanzapine, risperidone and older antipsychotics.

Method: We conducted a content analysis of an Internet database of comments about prescribed medications.

Results: We analysed 223 comments on risperidone, 170 on olanzapine and 46 relating to three older antipsychotics. The predominant subjective effects produced by all drugs consisted of sedation, cognitive impairment and emotional flattening or indifference. Connections appeared between these effects and Parkinsonian-like symptoms with the older drugs, sexual impairment with risperidone and metabolic effects with olanzapine. The experience of akathisia was frequently linked to suicidal thoughts. Some respondents described how the drugs’ subjective effects helped to reduce symptoms of mania, psychosis and anxiety.

Conclusion: The generalisability of Internet data is uncertain. However, the data suggest that adverse subjective effects play a central role in the experience of taking antipsychotic drugs and may be related to the drugs’ desired benefits.

Significant outcomes

- Sedation, impaired cognition and emotional flattening and indifference were most frequently associated with all the drugs examined. Few respondents mentioned pleasant effects such as calmness or relaxation.
- Although, the main subjective effects were shared by the different antipsychotics, they were associated with a different profile of physical effects.
- Some respondents described a beneficial impact of the main subjective mental effects of the antipsychotic drugs on their psychiatric symptoms.

Limitations

- The generalisability of data from Internet users is uncertain, and a bias towards negative comments may exist. However, the demographic and clinical profile of respondents resembles that of recipients of out-patient prescriptions of antipsychotics.
- Little information on dose or concurrent medications was available.
- We could not assess the prevalence of subjective effects since the website contained no prompt to disclose particular effects.

Introduction

Antipsychotic drugs are being prescribed with increasing frequency to people with an expanding variety of diagnoses (1). Although, their physical effects have been well characterised, their subjective effects, in particular the mental alterations they produce, are less well recognised. Their mechanism
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of action has also not been clarified. Early investigators noted the striking ability of the first such drugs to produce a subjective state characterised by mental slowing, apathy and emotional indifference (2, 3). Subsequent studies with volunteers and first person accounts by patients also emphasise the emotional detachment, reduced initiative, dysphoria and akathisia produced by these drugs (4–7).

Over the years, various labels have been used to describe these effects, including ‘neuroleptic induced dysphoria’ (8), ‘akinetic depression’ (9), ‘neuroleptic induced deficit syndrome’ (10), and ‘behavioural toxicity’ (11, 12).

There is increasing recognition of the importance of obtaining patients’ views about their problems and their treatment (13). However, few studies have investigated the experience of taking psychiatric medication from the perspective of the patient. Studies focusing on adverse effects have observed that the adverse mental effects of antipsychotics are frequent (14, 15) and often experienced as more unpleasant than the physical effects (16, 17). Research also shows that a negative experience of drug treatment is associated with poor quality of life (18–20) and with poor compliance (21–23).

Despite this research, the nature of the subjective state produced by antipsychotics has not been systematically described. Reports of the characteristic state associated with the older antipsychotics remain largely anecdotal and no comparable literature exists for the newer drugs. Since their profile of extrapyramidal and other physical effects appears to differ from that of the older drugs, the subjective effects they induce may also differ. Some studies suggest that, in comparison with the older drugs, the newer drugs are subjectively less aversive (24–27) and associated with a better quality of life (24, 28). However, recent randomised naturalistic trials have suggested no difference in quality of life or extra pyramidal effects (29, 30).

The subjective effects of antipsychotics drugs may also offer clues to their mechanism of action. Some investigators have proposed that ‘psychic indifference’ accounts for therapeutic effects in psychosis (31, 32), and recent research also suggests that antipsychotics reduce the intrusiveness and emotional impact of psychotic symptoms, rather than remove them altogether (33). This suggests that the drugs’ therapeutic effects are not specific to psychotic symptoms but rather may result from a general impact on cognition and emotion. Imaging studies suggest that the propensity of antipsychotic drugs to block dopamine D2 receptors – thought to be responsible for therapeutic effects – may also explain their ability to induce dysphoria (34–36). Again, this suggests there may be a link between the drugs’ subjective effects and their therapeutic potential.

Aims of the study

To describe and compare the subjective effects produced by taking different sorts of antipsychotic drugs. We have focused on the subjective mental alterations produced by the drugs, because it is these that have been most neglected, and we looked for evidence of both positive and negative drug-induced effects. We were also interested in how these mental effects related to the drugs’ physical effects.

Material and methods

We examined data from an Internet site that compiles uncensored user comments on the effects of taking different sorts of medication from people with a range of diagnoses. We conducted a qualitative and quantitative analysis of comments about the subjective experiences associated with taking two of the most widely prescribed new generation drugs, olanzapine and risperidone and the older neuroleptics. We also examined the occurrence of common physical effects such as extrapyramidal side effects and weight gain. In addition, we looked for information about how the characteristic subjective effects of antipsychotics interacted with the symptoms for which people were treated. On the http://www.askapatient.com website, people can record comments about a range of medicines which they are taking or have taken, including many drugs used in psychiatry. Two fields are available for authors (whom we will call ‘respondents’ for ease of writing) to enter discursive comments: one is titled ‘Side effects’ and the other, ‘Comments’. In both fields, respondents might typically write between 25 and 100 words. Respondents are also asked to enter some basic demographic information in separate fields, including their age, gender, diagnosis and the length of time they have been taking the drug. Although they are not asked for the dose, nor to name other drugs they might be taking concurrently, some respondents provide such details. Finally, respondents are asked to rate the drug on a scale from 1 (most negative) to 5 (most positive).

All data on http://www.askapatient.com are publicly available and anonymous, and posting a comment on a drug does not require respondents to register, although they may disclose their email address. We thus considered these communications analogous to public records or archives. Given their anonymous nature, and the website’s privacy
policy, we judged it ethically acceptable to conduct a passive analysis of the comments without seeking informed consent from their authors (37). Unfortunately, we could not determine the identity of the person or organisation who has constructed the website, or its source of funding or objectives, despite repeated requests.

Before the respondents’ entries were scrutinised, the authors compiled a list of possible subjective experiences associated with taking antipsychotic drugs derived from the known side effect profiles of different antipsychotics and from published first person accounts. All comments from http://www.askapatient.com on the drugs selected for this study were then printed and numbered consecutively. Two authors (JM and JPM) went through the comments initially, independently, to identify recurrent themes. This examination was not conducted blind to the drug type. The provisional list of possible effects was used as a guide, but additional effects and experiences were identified during inspection of the comments. A final list of effects and experiences was produced by consensus after discussion between the two authors involved in this process. The list focused on any altered experiences that could be attributed to the drugs. It excluded comments relating only to psychiatric symptoms, but links between subjective effects produced by the drugs and symptom changes were noted. Common reported physical effects were also assessed. One author (JM) then coded all the comments according to the final list of effects. Another author (JPM) replicated the coding process for all the comments for the older antipsychotics and the first 30 consecutive comments each for olanzapine and risperidone. A reliability test using kappa statistics then compared both authors’ coding.

To compare the effects associated with the different drugs, we noted the number of comments which mentioned each category of effect. Chi-square tests were then used to make three way comparisons between the older antipsychotics, risperidone and olanzapine (Table 2).

To illustrate the main categories of effects, we selected excerpts from individual comments which we felt exemplified or clarified the effects described and the relation between them (Table 3). Where expressed, we recorded respondents’ beliefs about how their altered experiences may have helped their symptoms. When any verbatim excerpts are presented below, they are identified by the consecutive case number we assigned to each individual respondent. The complete database we used in this study, including the case numbers, is available from the first author upon request.

### Results

Three older antipsychotic drugs used in psychiatric practice were covered by the database: chlorpromazine, trifluoperazine and haloperidol. After removing repeat entries and entries submitted by relatives, we counted nine first person comments for chlorpromazine, seven for trifluoperazine and 26 for haloperidol in the database on 17 August 2007, when data were retrieved for analysis. Three further comments for haloperidol and one for

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**Table 1. Demographic characteristics and drug ratings of respondents, by drugs rated**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Older antipsychotics* (n = 46)</th>
<th>Risperidone (n = 223)</th>
<th>Olanzapine (n = 170)</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number women (%)</td>
<td>24 (52.2)</td>
<td>127 (57.0)</td>
<td>93 (54.7)</td>
<td>( \chi^2 = 0.33 ) (2), ( P = 0.85 )</td>
</tr>
<tr>
<td>Mean age in years (SD)</td>
<td>36.3 (13.1)</td>
<td>30.7 (10.5)</td>
<td>34.1 (10.6)</td>
<td>( F = 7.43 ) (2), ( P = 0.001 ) Kruskall–Wallis</td>
</tr>
<tr>
<td>Mean duration of treatment in days (SD)</td>
<td>776.4 (1507.7)</td>
<td>609.9 (1043.5)</td>
<td>464.5 (837.9)</td>
<td>4.55 (2), ( P = 0.10 )</td>
</tr>
<tr>
<td>Mean daily dose in mg (SD)</td>
<td>46.5 (3.8)</td>
<td>2.2 (1.7)</td>
<td>11.3 (9.4)</td>
<td></td>
</tr>
<tr>
<td>Mean overall drug rating (SD) (range)</td>
<td>2.37 (1.67)</td>
<td>2.70 (1.45)</td>
<td>2.75 (1.48)</td>
<td>Kruskall–Wallis</td>
</tr>
<tr>
<td>Distribution of drug ratings</td>
<td>4 and 5</td>
<td>26%</td>
<td>31%</td>
<td>( \chi^2 = 1.4 ), df 4, ( P = 0.84 )</td>
</tr>
<tr>
<td>3</td>
<td>17%</td>
<td>20%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>1 and 2</td>
<td>57%</td>
<td>49%</td>
<td>49%</td>
<td></td>
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</tbody>
</table>

| Recorded diagnoses (%)           | Psychosis / schizophrenia       | 17 (37)               | 73 (32.7)            | 39 (22.9) | \( \chi^2 = 4.68 \) (2), \( P = 0.10 \) |
|                                  | Bipolar disorder                | 7 (15.2)              | 63 (28.3)            | 69 (40.6) | \( \chi^2 = 13.2 \) (2), \( P = 0.001 \) |
|                                  | Depression                      | 2 (4.3)               | 20 (9.0)             | 26 (15.3) | \( \chi^2 = 6.25 \) (2), \( P = 0.04 \) |
|                                  | Anxiety Disorders               | 3 (6.5)               | 21 (9.4)             | 17 (10.0) | \( \chi^2 = 0.52 \) (2), \( P = 0.77 \) |

*These included chlorpromazine (n = 9), trifluoperazine (n = 8), and haloperidol (n = 29).

†In haloperidol equivalents.
trifluoperazine posted later in the year were added to increase the sample size. Data on these three drugs were combined, since there were too few comments to make reliable distinctions between the drugs and upon inspection the comments revealed no notable differences. This yielded 46 responses concerning the older drugs. Also as of 17 August 2007, we counted 176 entries for olanzapine, of which 170 were first person accounts. There were 256 entries for risperidone (223 first person).

Comparative overview of reported drug effects

Table 1 shows demographic and clinical characteristics of the respondents according to the drugs they reported taking, and overall numerical rating of the drugs according to the website’s 5-point rating scale. Most respondents were female. Those taking the older antipsychotics were older ($P = 0.001$) and had been taking their drug for longer, although this difference was not statistically significant ($P = 0.10$). Between 23% and 33% of respondents recorded a diagnosis of psychosis or schizophrenia. Information on dose was only provided in 21–31% of comments, and daily doses were toward the lower end of the therapeutic range for all drug types. Overall ratings were slightly more positive for both newer antipsychotics, but the difference was not statistically significant ($P < 0.20$). When ratings for the two newer drugs were combined, a Mann–Whitney $U$-test produced a $Z$-value of 1.64 ($P = 0.10$).

Table 2 lists the final agreed-upon categories of effects. Kappa statistics measuring the magnitude of agreement between the two raters exceeded 0.8 for all categories except ‘euphoria’ (0.68), and all were statistically significant ($P < 0.001$).

Table 2 gives the proportion of respondents coded as mentioning each sort of effect at least once and results of Chi-square tests of the difference between the distributions of effects among the three types of drug. The most commonly reported effects across all three types of drug were sedation, subjective feelings of cognitive impairment and emotional flattening and loss of interest. Sedation was most commonly recorded for olanzapine while the older antipsychotics were associated with the most frequent complaints of cognitive dysfunction. A small number of people (<5%) taking each sort of drug reported positive mental alterations such as feelings of euphoria, or pleasant feelings of calmness or relaxation (most common with olanzapine), but numbers were too small for valid comparisons.

All three types of drug were reported as inducing depressive and suicidal symptoms by some respondents. We observed that suicidal thoughts were strongly associated with reporting akathisia: 13.8% of respondents reporting akathisia also reported suicidal thoughts, compared with 1.5% of those who did not mention akathisia ($\chi^2 = 20.8$, df = 1, $P < 0.001$). This association was accounted for predominantly by people taking olanzapine ($\chi^2 = 46.7$, df = 1, $P < 0.001$). Among people taking risperidone the results were weaker and not statistically significant ($\chi^2 = 3.12$, df = 1, $P = 0.08$) and no association was
observed among people taking older neuroleptics ($\chi^2 = 0.66$, df = 1, $P = 0.42$).

Mentions of well-recognised physical effects were distributed across the drugs as expected. Thus, Parkinsonian symptoms ($P < 0.001$) and akathisia ($P < 0.001$) were reported more commonly by people taking older neuroleptics. In contrast, weight gain was more frequently mentioned by people taking the newer drugs ($P < 0.001$), most frequently by people taking olanzapine. The category of 'extreme weight gain' comprises respondents who used terms like 'extreme', 'excessive' or 'huge' or who provided quantitative data indicating a weight increase of more than 2 kg (4 lbs) a month or 15 kg (30 lbs) in total. People taking olanzapine had the highest proportion of respondents (28.8%) whose comments fit these criteria. Cravings for sweet or 'junk' foods were also associated with taking olanzapine. Fourteen people taking olanzapine reported such effects, compared with only one on risperidone and none on the older drugs ($\chi^2 = 19.54$, df = 2, $P < 0.001$).

Of note, hormonal effects such as breast growth and lactation were only mentioned by people taking risperidone ($P < 0.001$) and sexual impairment such as loss of libido and impotence was mentioned more often by people taking risperidone ($P < 0.001$).
Qualitative descriptions of effects

Verbatim comments illustrating the nature of the subjective effects induced by the three types of drugs are listed in Table 3. Regardless of drug type, the sedative effects were described as profound and disabling by many respondents. Impaired cognitive abilities reported included reduced or slowed mental processes, mental clouding and feelings of reduced intelligence. All drugs induced similar emotional effects, which included feelings of flattened or numbed emotions, loss of interest and motivation, reduced creativity and perceived changes in personality.

Descriptions of extrapyramidal effects emphasised the connection between their physical and mental components. Comments on risperidone linked the sexual impairments to its mental effects and respondents taking olanzapine especially highlighted the connection between its metabolic effects (e.g. increased appetite) and its subjective mental effects (e.g. sedation and indifference). Although akathisia was less commonly cited in comments concerning olanzapine, four respondents explicitly associated it with the experience of suicidal thoughts (69, 233, 268, 271) in contrast to one comment on risperidone (23) and none on the older drugs. Terms such as ‘zombie’, ‘brainwashed’ and ‘braindead’ were used to describe the overall impact of taking antipsychotics by four respondents taking the older drugs (9%), 26 (11.7%) taking risperidone and 23 (13.5%) taking olanzapine.

Effects on psychiatric symptoms

For each type of drug, small numbers of respondents mentioned how the subjective effects described above produced improvement in their mental condition. The sedation produced by the drugs was cited as being useful by a number of respondents, especially those taking olanzapine. A woman who gave a diagnosis of insomnia commented how ‘the drug saved my life by getting me sleep so my nervous system could rest’ (O67). Some respondents linked improvements in their symptoms to feelings of calm produced by the drugs. A woman with schizoaffective disorder described how olanzapine produced ‘hypersomnia (increased sleeping), calming of moods, general smoothing out of mania, calmness, less hallucinations’ (O244). The ability of the drugs to slow down mental processes was also identified as important. One man diagnosed with bipolar I disorder, for example, described how he thought haloperidol had ‘decreased brain activity, slowed down racing thoughts’ (H127).

Others described how the medication decreased the intensity, intrusiveness or emotional impact of psychotic symptoms or unwelcome thoughts. A respondent taking risperidone described how it ‘decreased the intensity of inner voices’ (R216). A man who was taking olanzapine for schizoaffective disorder said ‘it really does well at keeping unwanted and persistent thoughts out of my head’ (O280). A young woman with anxiety, paranoia and self-harm described how the drug ‘stops my negative thoughts and feelings being amplified and overwhelming me’ (R326). A man with paranoid schizophrenia wrote how risperidone had ‘numbed my brain from psychotic thoughts, flattened most of my emotions’ (R391). A woman with anxiety and depression described how she felt olanzapine provided a ‘nice “buffer” between my anxiety/emo- tions and the outside world.’ (O110). Another woman with depression described how taking olanzapine made her ‘less sensitive to perceived rejection’ (O93). Two respondents taking olanzapine commented that it had reduced suicidal thoughts (O91, O245).

Several respondents linked the loss of interest induced by the drugs with beneficial effects. A woman who had taken haloperidol for ‘delirium and hallucination’ linked this effect with being more in contact with reality: ‘Although I felt very well, I felt as if I had absolutely nothing to talk about. I kept wondering about whatever [it] was that had been so interesting during most of my life that I had suddenly lost… But I was very much in contact with reality and for that I was thankful’ (H134). A man who took risperidone for anxiety commented that the drug ‘reduced my excessive worrying, but now I don’t seem to care much about anything anymore’ (R392).

Several comments captured the difficult balance between the negative impact of the drugs and the improvement of symptoms. One woman with
psychosis commented that taking olanzapine ‘makes me feel like a veggie, but that was better than what I was going through and it kept me out of the hospital’ (O61).

**Discussion**

Limitations of the current study

A concern with using data from a website is that users may be motivated to access it because of unusually negative experiences with prescribed drugs. As Internet users are a self-selected sample, it is also difficult to know how representative they are of general users of antipsychotic medication. The website http://www.askapatient.com is designed to provide information about people’s experiences with drugs, and is not wholly concerned with adverse effects, but it does contain a column for recording ‘side effects’. However, most respondents wrote more in the field labelled ‘Comments’ than in the field labelled ‘Side effects’. In addition, the nature of the effects identified in this data set is consistent with those identified in conventional prevalence studies. These questionnaire-based studies find up to half of subjects complaining of sedation or concentration difficulties and a third or more reporting emotional flattening or depression (14, 15, 38, 39) – higher rates of subjective adverse effects than reported by this sample. Moreover, the numerical ratings of the drugs’ effects on http://www.askapatient.com also indicate that many users found them helpful overall, with around half of respondents giving the drugs a positive or middle rating (Table 1). Finally, the fact that respondents had been taking the drugs for at least a year on average, suggests they were not the most dissatisfied people who might stop treatment immediately. In sum, although Internet users might be more disgruntled than general medication users, we saw no particular indications of this in the current data or from comparisons with other research.

People who use the Internet are more likely to be middle class and younger than the general population, although users of http://www.askapatient.com are older than average Internet users (http://www.quantcast.com/askapatient, accessed 30 March 2008). Also, people other than genuine users of medications may have contributed comments (40). Dose was recorded infrequently, and where it was doses were at the lower end of the usually recommended therapeutic range. In contrast, most respondents had used medication for a considerable time, reflecting common clinical practice. Few people recorded the use of concur-
Implications of results

Consistent with previous research, the present study found that subjective mental alterations were among the most commonly described type of adverse effect of antipsychotic drugs (14, 38). The data suggest that different types of antipsychotics produce strikingly similar emotional, motivational and cognitive effects. All appear to produce a state characterised by sedation, flattening of emotional responses, indifference and impaired subjective cognitive functioning. However, for older drugs the subjective state is connected to Parkinsonism, consisting of feelings of slowness, rigidity and difficulty with movement, less prominent with the two newer drugs. For risperidone, the subjective effects are associated with sexual impairment, particularly loss of libido and impotence. In the case of olanzapine, respondents linked increase in appetite and weight gain with the characteristic mental changes produced by the drug. All three drugs produced akathisia, with fewer reports from people on the newer drugs. Akathisia was strongly associated with reporting suicidal thoughts, especially in people taking olanzapine. Some respondents specifically described how the intolerability of akathisia led to thoughts of suicide.

It has long been recognised that antipsychotics produce unpleasant effects in many people (8, 16). The effects described here were strongly disliked by some respondents, illustrated by comments such as ‘horrible stuff’ (chlorpromazine, 158), ‘living hell’ ( risperidone, 16) and ‘if you would not willingly undergo a lobotomy, then do not take this drug’ (olanzapine, 77). Consistent with some previous studies (26), numerical ratings suggested the newer drugs were slightly better liked than the older ones, but the difference was not statistically significant. However, some respondents’ comments also suggested that cognitive slowing, reduced mental activity and emotional flattening helped suppress or improve psychiatric symptoms such as racing thoughts, delusions, hallucinations and anxiety. These observations strengthen the suggestion that part of the desired, therapeutic effect of antipsychotic drugs is obtained from non-specific, and usually adversely experienced, effects on mental functioning as a whole (32, 43).

Findings on the role of D2 blockade in producing dysphoria (35, 44, 45) would be consistent with this thesis, since D2 blockade is thought to be responsible for both therapeutic effects and extrapyramidal effects at higher levels. However, the different physical effects associated with the subjective effects produced by the drugs examined here suggest that different mechanisms may produce a similar drug-induced state. The comments on olanzapine, for example, suggest that increased appetite and metabolic effects are intrinsically related to the emotional and cognitive effects of the drug. As the metabolic effects of olanzapine are not thought to be attributable to D2 blockade, it appears that pharmacological mechanisms other than D2 receptor occupancy may be involved in producing its subjective effects. Consistent with this thesis, data from one randomised study of olanzapine and haloperidol indicated that D2 blockade influenced subjective well-being only in haloperidol treated subjects (44). However, another imaging study found a relation in olanzapine-treated patients as well, using higher doses in some subjects (35).

Studies have found that clinicians ignore or minimise patients’ complaints about the negative subjective effects of antipsychotics (46). The current findings show that these effects loom large in the overall drug experience and that patients face a difficult trade off between a possible reduction of symptoms and a mostly unpleasant drug-induced state. This state probably accounts for some of the finding that most chronic psychotic patients cease taking older and newer antipsychotic medications within 18 months of starting them (47). To improve patients’ experience, doses of antipsychotics should be kept as low as possible and further use could be made of drugs that produce less aversive effects such as benzodiazepines. Treatment approaches that attempt to avoid or minimise the use of antipsychotics could also be explored further, given promising results from some studies (48). Overall, prescribers need to take subjective effects of medications seriously and doctors and their patients need more information about the nature of these effects in order to make informed judgements about their use.

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