

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.

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Key words: antipsychotic agents; side effects; psychopharmacology; patient-centred research; subjective effects of drugs

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Accepted for publication January 16, 2009

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

1 of action has also not been clarified. Early inves-
2 tigators noted the striking ability of the first such
3 drugs to produce a subjective state characterised by
4 mental slowing, apathy and emotional indifference
5 (2, 3). Subsequent studies with volunteers and first
6 person accounts by patients also emphasise the
7 emotional detachment, reduced initiative, dyspho-
8 ria and akathisia produced by these drugs (4–7).
9 Over the years, various labels have been used to
10 describe these effects, including ‘neuroleptic
11 induced dysphoria’ (8), ‘akinetic depression’ (9),
12 ‘neuroleptic induced deficit syndrome’ (10), and
13 ‘behavioural toxicity’ (11, 12).

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

26 Despite this research, the nature of the subjective
27 state produced by antipsychotics has not been
28 systematically described. Reports of the character-
29 istic state associated with the older antipsychotics
30 remain largely anecdotal and no comparable liter-
31 ature exists for the newer drugs. Since their profile
32 of extrapyramidal and other physical effects
33 appears to differ from that of the older drugs, the
34 subjective effects they induce may also differ. Some
35 studies suggest that, in comparison with the older
36 drugs, the newer drugs are subjectively less aversive
37 (24–27) and associated with a better quality of life
38 (24, 28). However, recent randomised naturalistic
39 trials have suggested no difference in quality of life
40 or extra pyramidal effects (29, 30).

41 The subjective effects of antipsychotics drugs
42 may also offer clues to their mechanism of action.
43 Some investigators have proposed that ‘psychic
44 indifference’ accounts for therapeutic effects in
45 psychosis (31, 32), and recent research also sug-
46 gests that antipsychotics reduce the intrusiveness
47 and emotional impact of psychotic symptoms,
48 rather than remove them altogether (33). This
49 suggests that the drugs’ therapeutic effects are not
50 specific to psychotic symptoms but rather may
51 result from a general impact on cognition and
52 emotion. Imaging studies suggest that the propen-
53 sity of antipsychotic drugs to block dopamine D₂
54 receptors – thought to be responsible for thera-
55 peutic effects – may also explain their ability to
56 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, includ-
ing 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 respon-
dents 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

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

Characteristics	Older antipsychotics* (n = 46)	Risperidone (n = 223)	Olanzapine (n = 170)	Test
Number women (%)	24 (52.2)	127 (57.0)	93 (54.7)	$\chi^2 = 0.33$ (2), $P = 0.85$
Mean age in years (SD)	36.3 (13.1)	30.7 (10.5)	34.1 (10.6)	$F = 7.43$ (2), $P = 0.001$
Mean duration of treatment in days (SD)	776.4 (1507.7)	609.9 (1043.5)	464.5 (837.9)	Kruskall-Wallis 4.55 (2), $P = 0.10$
Mean daily dose in mg (SD)	†6.5 (3.8) range 1.5–13.3 (n = 11)	2.2 (1.7) range 0.25–7 (n = 68)	11.3 (9.4) range 3–20 (n = 35)	
Mean overall drug rating (SD) (5 most positive, 1 most negative)	2.37 (1.67)	2.70 (1.45)	2.75 (1.48)	Kruskall-Wallis 2.68 (2), $P = 0.26$
Distribution of drug ratings				
4 and 5	26%	31%	34%	$\chi^2 = 1.4$, df 4, $P = 0.84$
3	17%	20%	18%	
1 and 2	57%	49%	49%	
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.

Table 2. Main categories of subjective and physical effects associated with older antipsychotics, risperidone and olanzapine

Category of effect	Number (percentage) of respondents			Chi-squared (degrees of freedom)
	Older antipsychotics (<i>n</i> = 46)	Risperidone (<i>n</i> = 223)	Olanzapine (<i>n</i> = 170)	
Sedative effects (increased sleep, daytime drowsiness, fatigue, lethargy, difficulty waking)	20 (43.5)	93 (41.7)	95 (55.9)	8.09 (2), <i>P</i> = 0.017
Cognitive effects (impaired concentration or memory, mental slowness)	16 (34.8)	41 (18.4)	29 (17.1)	7.64 (2) <i>P</i> = 0.022
Motivational and emotional effects (flattened emotions, indifference, loss of interest, change of personality, loss of creativity)	9 (19.6)	48 (21.5)	37 (21.8)	0.107 (2) <i>P</i> = 0.95
Parkinsonian effects (stiffness, slowness and heaviness)	15 (32.6)	22 (9.9)	6 (3.5)	34.65 (2), <i>P</i> < 0.001
Akathisia (mental or physical restlessness and tension)	11 (23.9)	16 (7.2)	9 (5.3)	17.31 (2) <i>P</i> < 0.001
Anxiety/irritability	4 (8.7)	20 (9.0)	9 (5.3)	1.98 (2), <i>P</i> = 0.37
Depression	2 (4.3)	9 (4.0)	10 (5.9)	0.743 (2), <i>P</i> = 0.69
Suicidal thoughts (attributed to drug)	2 (4.3)	3 (1.4)	6 (3.5)	2.60 (2), <i>P</i> = 0.27
Euphoria, relaxation and calmness	1 (2.2)	7 (3.1)	8 (4.7)	0.991 (2), <i>P</i> = 0.609
Sexual impairment	1 (2.2)	59 (26.5)	9 (5.3)	39.73 (2), <i>P</i> < 0.001
Hormonal effects	0	30 (13.5)	0	31.19 (2), <i>P</i> < 0.001
Weight gain	5 (10.9)	82 (36.8)	88 (51.8)	27.07 (2), <i>P</i> < 0.001
Extreme weight gain	2 (4.3)	30 (13.5)	49 (28.8)	21.94 (2), <i>P</i> < 0.001
Increased appetite or food cravings	0	19 (8.5)	43 (25.3)	30.83 (2), <i>P</i> < 0.001

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

Table 3. Verbatim qualitative data excerpts on subjective effects

Effect	Typical comments
Sedative effects	'I'm still fatigued in the morning and can barely get out of bed some days' (T144) 'I feel tired all the time. Too tired to be depressed' (R316) 'I was sleeping over 14 h a night and was so hung over during the day I could hardly go about my normal routines. I couldn't even get myself dressed to go out to the store' (O235).
Cognitive effects	'low ability to make decisions' (T146) 'no thoughts or inner world' (R356) 'mental fogginess all the time' (R1) 'altered mental state, cannot focus. Impaired judgement and thinking' (R372) 'blank mind' (O89) 'sluggish thinking' (O112) 'loss of wits' (O276)
Emotional effects	'I feel absolutely nothing!! No sadness, no joy, NOTHING' (H119) 'emotionally empty, dead inside... took away my sense of humour' (T150) 'oblivious to my surrounds....all creativity was squashed' (T145) 'no emotions, only a weird, spacey, empty feeling, no arousal, no excitement, no joy, nothing' (R22) 'total shut down of my outgoing personality' (R181) 'emotionless zombie' (R392) 'lack of interest in life, no will to carry on living' (R16) 'too zoned, too robotic, emotion dead' (O97) 'lost of emotions and general feeling that everything doesn't matter at all' (O234). 'personality is dampened' (O107). 'general lack of interest in anything' (O291)
Parkinsonian effects	'..extremely hard to move, think, talk' (H121) 'I feel like a zombie, I can't think clear and my movement is slow' (119H) 'heavy mental and physical stagnance... retarded feeling' (H137) 'I felt like I was in slow motion' (R21) 'I am not able to think properly and am experiencing the world at about half the normal pace... Can't keep my mind focused and my eyes are slow' (O114). 'mild inhibited feeling' (O292).
Akathisia	'horrible restlessness' (H128) '..extreme physical agitation combined with a zombielike mind state' (C158) 'I felt like scratching my eyes out and my skin off and running into the walls' (R23) 'ineffable anxiety, which was sort of like restless leg syndrome' (R169) 'restlessness, the kind where you wanna kill yourself' (O233).
Euphoria or relaxation	'Makes me more relaxed and content' (O280) 'So far this has kept my mood balanced and given me a sense of calm I haven't had in a very long time' (R 11)
Sexual effects	'I lost my ability to feel emotions, I lost my libido, I lost my drives, I lost my ability to get an erection' (R22) 'Low motivation, narrow emotional range, can't get excited about things, libido and drive have been obliterated' (R178)
Metabolic effects	'ravenous, rapacious hunger that never quit' (O68) 'I feel numb, like I've been brainwashed. There is more to life than eating and sleeping' (O89) 'I've never been able to eat as much as I did when I was on Zyprexa. I gained 40lbs in no time and my mind was in a constant fog of lethargy and indifference. I didn't care about anything. I just wanted to sit around and eat' (O62) 'I was a humongous zombie on Zyprexa' (O68) 'I keep eating and eating and sleeping and sleeping and sometimes I manage to do both at the same time' (O251)

C, chlorpromazine; H, haloperidol; O, olanzapine; R, risperidone; T, trifluoperazine.

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 ($P < 0.001$).

Table 4. Characteristics of patients prescribed antipsychotics in the National Ambulatory Medical Care Survey (NAMCS) and in this Internet sample

	Older antipsychotics		Newer antipsychotics	
	NAMCS		NACMS	
	(unweighted <i>n</i> = 1546*)	Internet (<i>n</i> = 46)	(unweighted <i>n</i> = 3132*)	Internet (<i>n</i> = 393)
Mean age in years	49.4	36.3	46.4	32.2
% female	55.0	52.2	59.1	55.9
% diagnosed with psychosis or schizophrenia	51.2	37	32.9	28.5
% diagnosed with bipolar disorder	12.0	15.2	21.8	33.6
% diagnosed with depression	21.5	4.3	34.8	11.7
% diagnosed with anxiety	9.1	6.5	13.4	9.7

*Data points are visits rather than patients.

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/emotions 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

1 psychosis commented that taking olanzapine
2 'makes me feel like a veggie, but that was better
3 than what I was going through and it kept me out
4 of the hospital' (O61).

7 Discussion

8 Limitations of the current study

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

44 People who use the Internet are more likely to be
45 middle class and younger than the general popu-
46 lation, although users of <http://www.askapatient.com>
47 are older than average Internet users
48 (<http://www.quantcast.com/askapatient>, accessed
49 30 March 2008). Also, people other than genuine
50 users of medications may have contributed com-
51 ments (40). Dose was recorded infrequently, and
52 where it was doses were at the lower end of the
53 usually recommended therapeutic range. In con-
54 trast, most respondents had used medication for a
55 considerable time, reflecting common clinical
56 practice. Few people recorded the use of concur-

rent medications, which precludes attributing with
certainty the effects described to the antipsychotic
drugs. However, this reflects the clinical situation,
as more than 80% of people on antipsychotics are
prescribed other medications (1).

The latest data from the United States National
Ambulatory Medical Care Survey (NAMCS) show
a higher mean age of patients prescribed typical and
atypical antipsychotics compared with the current
sample, but in other respects the samples are
comparable (Table 3). The current sample of users
of the older drugs included a lower proportion of
people diagnosed with psychosis or schizophrenia
and among users of newer antipsychotics, there were
more people diagnosed with bipolar disorder and
considerably fewer with depression. This probably
reflects increasing trends in the diagnosis of bipolar
disorder (41). The NAMCS also found that between
a fifth and a third of prescriptions of antipsychotics
were issued by non-psychiatrists, and the volume of
prescribing by non-psychiatrists was increasing (1,
42). Thus, it appears that the current sample reflects
trends for antipsychotics to be prescribed to people
with an increasing variety of diagnoses.

A problem for the interpretation of all research
on subjective medication effects is the possibility
that users misinterpret symptoms of their mental
disorder as side effects. We only recorded effects
that were clearly believed by respondents to arise
from taking medication, but we cannot exclude the
possibility that some people misinterpreted the
origin of their experiences. However, that well
validated adverse effects, such as Parkinsonism and
hormonal effects were distributed among the dif-
ferent drugs as expected gives confidence that this
study draws a reasonably accurate picture of what
it is like to take antipsychotic drugs. In addition,
our distinction between some of the different
mental effects was somewhat artificial. Sedative,
cognitive and emotional effects are likely related,
but we have separated them to emphasise the
particular features of the state induced by these
antipsychotic drugs that may distinguish them
from other sorts of psychotropic drugs.

Finally, the current study could not assess the
prevalence of drug-related effects, as the website
contained no prompt to disclose particular effects.
Although some respondents appeared to list all the
effects they experienced, others mentioned only one
or two, without indicating whether or not others
were present. However, the spontaneous, open-
ended and uncensored format of the comments,
their existence independent of any research project,
as well as their considerable number, are unique
aspects of these data on subjective effects of taking
antipsychotic drugs.

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 pro-

duce 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.

References

1. SANKARANARAYANAN J, PUUMALA SE. Antipsychotic use at adult ambulatory care visits by patients with mental health disorders in the United States, 1996–2003: national estimates and associated factors. *Clin Ther* 2007;**29**:723–741.
2. LEHMANN HE, HANRAHAN GE. Chlorpromazine; new inhibiting agent for psychomotor excitement and manic states. *AMA Arch Neurol Psychiatry* 1954;**71**:227–237.
3. DENIKER P. Psychophysiological aspects of the new chemotherapeutic drugs in psychiatry. *J Nerv Ment Dis* 1957;**125**:427–431.
4. BELMAKER RH, WALD D. Haloperidol in normals. *Br J Psychiatry* 1977;**131**:222–223.
5. HEALY D, FARQUHAR G. Immediate effects of droperidol. *Hum Psychopharmacol* 1998;**13**:113–120.
6. RAMAEKERS JG, LOUWERENS JW, MUNTJEWERFF ND et al. Psychomotor, Cognitive, extrapyramidal, and affective functions of healthy volunteers during treatment with an

- atypical (amisulpride) and a classic (haloperidol) antipsychotic. *J Clin Psychopharmacol* 1999;**19**:209–221.
7. WALLACE M. Schizophrenia – a national emergency: preliminary observations on SANELINE. *Acta Psychiatr Scand Suppl* 1994;**380**:33–35.
 8. AWAD AG, VORUGANTI LN. Neuroleptic dysphoria: revisiting the concept 50 years later. *Acta Psychiatr Scand Suppl* 2005;**427**:6–13.
 9. VAN PUTTEN T, MAY PRA. Subjective response as a predictor of outcome in pharmacotherapy; the consumer has a point. *Arch Gen Psychiatry* 1978;**35**:477–480.
 10. LADER M. Neuroleptic-induced deficit syndrome. Historical introduction. *Acta Psychiatr Scand Suppl* 1994;**380**:6–7.
 11. HOLLISTER LE. Complications from the use of tranquilizing drugs. *N Engl J Med* 1957;**257**:170–177.
 12. VAN PUTTEN T, MARDER SR. Behavioral toxicity of antipsychotic drugs. *J Clin Psychiatry* 1987;**48**(Suppl.):13–19.
 13. GEEKIE J. Listening to the voices we hear: clients understanding of psychotic experiences. In: READ J, MOSHER LR, BENTALL RP, eds. *Models of madness*. Hove, East Sussex: Brunner-Routledge, 2004:147–160.
 14. BARBUI C, NOSE M, BINDMAN J et al. Sex differences in the subjective tolerability of antipsychotic drugs. *J Clin Psychopharmacol* 2005;**25**:521–526.
 15. HOFER A, RETTENBACHER MA, EDLINGER M, KEMMLER G, WIDSCHWENDTER CG, FLEISCHHACKER WW. Subjective response and attitudes toward antipsychotic drug therapy during the initial treatment period: a prospective follow-up study in patients with schizophrenia. *Acta Psychiatr Scand* 2007;**116**:354–361.
 16. VAN PUTTEN T. Why do schizophrenic patients refuse to take their drugs? *Arch Gen Psychiatry* 1974;**31**:67–72.
 17. AWAD AG. Subjective response to neuroleptics in schizophrenia. *Schizophr Bull* 1993;**19**:609–618.
 18. BROWNE S, GARAVAN J, GERVIN M, ROE M, LARKIN C, O'CALLAGHAN E. Quality of life in schizophrenia: insight and subjective response to neuroleptics. *J Nerv Ment Dis* 1998;**186**:74–78.
 19. HOFER A, KEMMLER G, EDER U, EDLINGER M, HUMMER M, FLEISCHHACKER WW. Quality of life in schizophrenia: the impact of psychopathology, attitude toward medication, and side effects. *J Clin Psychiatry* 2004;**65**:932–939.
 20. AWAD AG, HOGAN TP. Subjective response to neuroleptics and the quality of life: implications for treatment outcome. *Acta Psychiatr Scand Suppl* 1994;**380**:27–32.
 21. HOGAN TP, AWAD AG, EASTWOOD R. A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. *Psychol Med* 1983;**13**:177–183.
 22. NABER D. A self-rating to measure subjective effects of neuroleptic drugs, relationships to objective psychopathology, quality of life, compliance and other clinical variables. *Int Clin Psychopharmacol* 1995;**10**(Suppl. 3): 133–138.
 23. GARAVAN J, BROWNE S, GERVIN M, LANE A, LARKIN C, O'CALLAGHAN E. Compliance with neuroleptic medication in outpatients with schizophrenia; relationship to subjective response to neuroleptics; attitudes to medication and insight. *Compr Psychiatry* 1998;**39**:215–219.
 24. RITSNER M, GIBEL A, PERELROYZEN G, KURS R, JABARIN M, RATNER Y. Quality of life outcomes of risperidone, olanzapine, and typical antipsychotics among schizophrenia patients treated in routine clinical practice: a naturalistic comparative study. *J Clin Psychopharmacol* 2004;**24**:582–591.
 25. AWAD AG, VORUGANTI LN. New antipsychotics, compliance, quality of life, and subjective tolerability – are patients better off? *Can J Psychiatry* 2004;**49**:297–302.
 26. NABER D, MORITZ S, LAMBERT M et al. Improvement of schizophrenic patients' subjective well-being under atypical antipsychotic drugs. *Schizophr Res* 2001;**50**:79–88.
 27. VORUGANTI L, CORTESE L, OYEWUMI L, CERNOVSKY Z, ZIRUL S, AWAD A. Comparative evaluation of conventional and novel antipsychotic drugs with reference to their subjective tolerability, side-effect profile and impact on quality of life. *Schizophr Res* 2000;**43**:135–145.
 28. FRANZ M, LIS S, PLUDDMANN K, GALLHOFER B. Conventional versus atypical neuroleptics: subjective quality of life in schizophrenic patients. *Br J Psychiatry* 1997;**170**:422–425.
 29. JONES PB, BARNES TR, DAVIES L et al. Randomized controlled trial of the effect on Quality of Life of second- vs first-generation antipsychotic drugs in schizophrenia: Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1). *Arch Gen Psychiatry* 2006;**63**:1079–1087.
 30. MILLER dD, CAROFF SN, DAVIS SM et al. Extrapyramidal side-effects of antipsychotics in a randomised trial. *Br J Psychiatry* 2008;**193**:279–288.
 31. DENIKER P. Psychophysiological aspects of the new chemotherapeutic drugs in psychiatry; some practical features of neuroleptics in order to screen new drugs. *J Nerv Ment Dis* 1956;**124**:371–376.
 32. HEALY D. Neuroleptics and psychic indifference: a review. *J R Soc Med* 1989;**82**:615–619.
 33. MIZRAHI R, BAGBY RM, ZIPURSKY RB, KAPUR S. How antipsychotics work: the patients' perspective. *Prog Neuro-psychopharmacol Biol Psychiatry* 2005;**29**:859–864.
 34. VORUGANTI L, SLOMKA P, ZABEL P et al. Subjective effects of AMPT-induced dopamine depletion in schizophrenia: correlation between dysphoric responses and striatal D(2) binding ratios on SPECT imaging. *Neuropsychopharmacology* 2001;**25**:642–650.
 35. MIZRAHI R, RUSJAN P, AGID O et al. Adverse subjective experience with antipsychotics and its relationship to striatal and extrastriatal D2 receptors: a PET study in schizophrenia. *Am J Psychiatry* 2007;**164**:630–637.
 36. VORUGANTI LP, AWAD AG. Brain imaging research on subjective responses to psychotropic drugs. *Acta Psychiatr Scand Suppl* 2005;**427**:22–28.
 37. EYSENBACH G, TILL JE. Ethical issues in qualitative research on Internet communities. *BMJ* 2001;**323**:1103–1105.
 38. MORRISON P, GASKILL D, MEEHAN T, LUNNEY P, LAWRENCE G, COLLINGS P. The use of the Liverpool University Neuroleptic Side-Effect Rating Scale (LUNSERS) in clinical practice. *Aust N Z J Ment Health Nurs* 2000;**9**:166–176.
 39. ADEWUYA AO, OLA BA, MOSAKU SK, FATOYE FO, EEGUNRANTI AB. Attitude towards antipsychotics among outpatients with schizophrenia in Nigeria. *Acta Psychiatr Scand* 2006;**113**:207–211.
 40. O'NEIL A. The patient trust deficit in pharmaceutical marketing. *DTC Perspectives* 2007;December:12–16.
 41. MORENO C, LAJE G, BLANCO C, JIANG H, SCHMIDT AB, OLFSO M. National trends in the outpatient diagnosis and treatment of bipolar disorder in youth. *Arch Gen Psychiatry* 2007;**64**:1032–1039.
 42. APARASU RR, BHATARA V, GUPTA S. U.S. national trends in the use of antipsychotics during office visits, 1998–2002. *Ann Clin Psychiatry* 2005;**17**:147–152.
 43. BREGGIN PR. *Brain disabling treatments in psychiatry: Drugs electroshock and the role of the FDA*. New York: Springer Publishing Company, 1997.
 44. DE HAAN L, VAN BRUGGEN M, LAVALAYE J, BOOIJ J, DINGEMANS PM, LINSZEN D. Subjective experience and D2 receptor occupancy in patients with recent-onset schizophrenia treated with low-dose olanzapine or haloperidol: a ran-

- 1 domized, double-blind study. *Am J Psychiatry* 2003;**160**:
2 303–309.
- 3 45. DE HAAN L, LAVALAYE J, LINSZEN D, DINGEMANS PM, BOOIJ J.
4 Subjective experience and striatal dopamine D(2) receptor
5 occupancy in patients with schizophrenia stabilized by
6 olanzapine or risperidone. *Am J Psychiatry* 2000;**157**:1019–
7 1020.
- 8 46. SEALE C, CHAPLIN R, LELLIOTT P, QUIRK A. Antipsychotic
9 medication, sedation and mental clouding: an observa-
10 tional study of psychiatric consultations. *Soc Sci Med*
11 2007;**65**:698–711.
- 12 47. LIEBERMAN JA, STROUP TS, MCEVOY JP et al. Effectiveness of
13 antipsychotic drugs in patients with chronic schizophrenia.
14 *N Engl J Med* 2005;**353**:1209–1223.
- 15 48. CALTON T, FERRITER M, HUBAND N, SPANDLER H. A systematic
16 review of the Soteria paradigm for the treatment of people
17 diagnosed with schizophrenia. *Schizophr Bull* 2008;**34**:
18 181–192.
- 19
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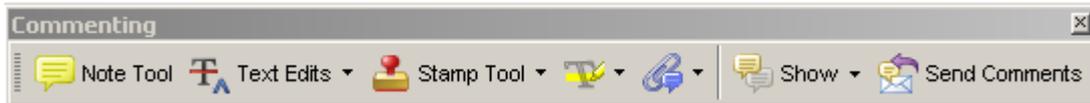
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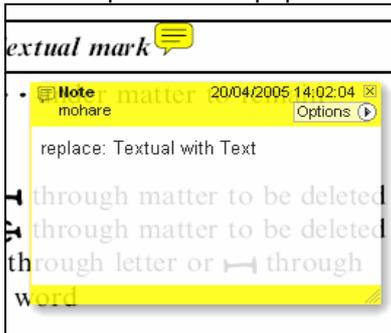
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Note Tool — For making notes at specific points in the text

Marks a point on the paper where a note or question needs to be addressed.

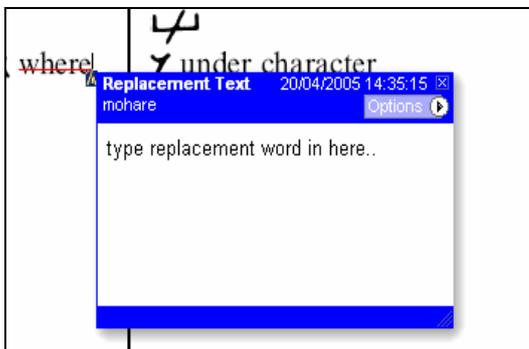


How to use it:

1. Right click into area of either inserted text or relevance to note
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Replacement text tool — For deleting one word/section of text and replacing it

Strikes red line through text and opens up a replacement text box.

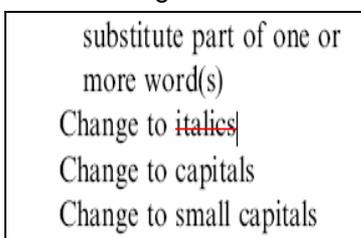


How to use it:

1. Select cursor from toolbar
2. Highlight word or sentence
3. Right click
4. Select Replace Text (Comment) option
5. Type replacement text in blue box
6. Click outside of the blue box to close

Cross out text tool — For deleting text when there is nothing to replace selection

Strikes through text in a red line.



How to use it:

1. Select cursor from toolbar
2. Highlight word or sentence
3. Right click
4. Select Cross Out Text

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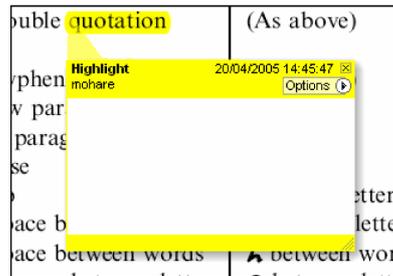


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1. Click on the Stamp Tool in the toolbar
2. Select the Approved rubber stamp from the 'standard business' selection
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Highlight tool — For highlighting selection that should be changed to bold or italic.

Highlights text in yellow and opens up a text box.

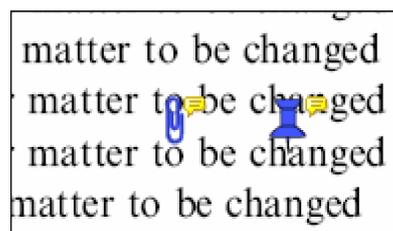


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2. Highlight the desired text
3. Add a note detailing the required change

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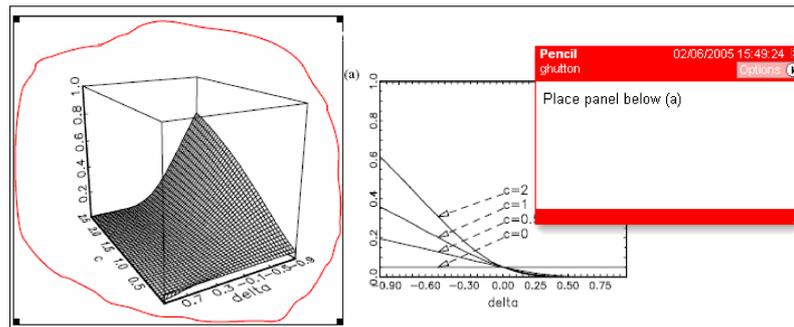


How to use it:

1. Click on paperclip icon in the commenting toolbar
2. Click where you want to insert the attachment
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Pencil tool — For circling parts of figures or making freeform marks

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How to use it:

1. Select Tools > Drawing Markups > Pencil Tool
2. Draw with the cursor
3. Multiple pieces of pencil annotation can be grouped together
4. Once finished, move the cursor over the shape until an arrowhead appears and right click
5. Select Open Pop-Up Note and type in a details of required change
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