Antipsychotic Medications, Psychological Side Effects and Treatment Engagement

Nev Jones, MA
Department of Psychology, DePaul University, Chicago, IL, USA

Patient complaints of antipsychotic-induced apathy, emotional indifference, mental “fogginess,” “blankness,” and “clouding,” among others, are undoubtedly familiar to practicing psychiatric clinicians. This “family” of subjective psychological side effects, variously dubbed “neuroleptic dysphoria” (Awad & Voruganti, 2005; Singh & Smith, 1976), “behavioral toxicity” (Hollister, 1957; Van Putten & Marder, 1987), and “neuroleptic-induced psychic indifference” (Healy, 1989; Kalinowsky, 1958) has been noted by clinicians and studied by researchers since the introduction of chlorpromazine in the 1950s.

Although dopamine has been suspected to play a role in this negative subjective “syndrome” for over half a century, direct links between dopamine antagonism—antipsychotics, primary mechanism of action—and dysphoria have been clarified only recently. As Awad and Voruganti (2005) detail, research regarding subjective dysphoria has mostly taken one of two approaches: (1) comparing correlations between side effects and rates of dopamine receptor occupancy, utilizing antipsychotics with differing receptor occupancy profiles (e.g., Kirsch, Ronshausen, Mier & Gallhofer, 2007; Mizrahi et al., 2007), and (2) using selective dopamine depleting drugs such as alpha-methyl-para-tyrosine (AMPT) to induce phenomenologically identical “neuroleptic dysphoria.” With respect to the second approach, Voruganti and colleagues (Voruganti & Awad, 2006; Voruganti et al., 2001) have used AMPT in medication-free schizophrenia patients to successfully trigger a cascade of negative affects beginning with anhedonia, “clouded thinking,” and amotivation and ultimately leading to social withdrawal and a state of explicit subjective distress. de Haan, Booij, Lavallye, van Amelsvoort, and Linszen (2005) have also produced AMPT-induced dysphoria in a health subject, documenting a similarly complex array and cognitive and behavioral effects.

The complexity of these effects—impacting emotion, cognition, motivation, and behavior—cannot be overemphasized, an unsurprising fact given the complexity and controversy regarding the functions of the striatal dopamine system. Thus researchers have variously argued that striatal dopamine plays a key role in hedonic response, reward, incentive motivation, motor dysfunction, addiction (for overviews see Wise, 2004, 2008), and possibly even “consciousness” itself (Palmiter, 2011).

Until scientific advances allow us to better unpack these functions and their relationships with greater precision, it is perhaps most illustrative to consider first-person descriptions of the functional and behavioral impact of neuroleptic dysphoria. In an early report, for example, the Israeli researchers Belmaker and Wald (1977) recounted their personal experiences following the injection of 5 mg of haloperidol as follows:

The effect was marked and very similar in both of us: within ten minutes a marked slowing of thinking and movement developed, along with profound inner restlessness. Neither [of us] could continue work, and each left work for over 36 hours. Each [of us] complained of a paralysis of volition, a lack of physical and psychic energy. [We] felt unable to read, telephone or perform household tasks of [our] own will, but could perform these tasks if demanded to do so. (p. 222)

Likewise, Healy and Farquhar’s (1998) non-patient volunteers described a complex mix of sedation, the feeling of increased effortfulness, affective dysphoria, poor concentration, and anergia. “There was a general feeling common to all subjects to some extent of disengagement—a feeling of uninvolvement with tasks in hand,” the authors summarize: even “apparently simple tasks, such as obtaining a sandwich from a sandwich machine, proved too difficult for some people” (p. 116).

In spite of the fact that patients are most often describing long-term rather than acute short-term side effects, their reports are strikingly similar. Descriptions reported in a novel Internet-based content analysis carried out by Moncrieff, Cohen, and Mason (2009) utilized such phrases as “blank mind,” “too zoned, too robotic, emotion dead,” “personality is dampened,” “low ability to make decisions,” and “sluggish wits.” A patient quoted in a qualitative study by Rogers et al. (1998) elaborated as follows:

Address correspondence to Nev Jones, Department of Psychology, DePaul University, Chicago, IL, 60614, USA. E-mail: nev.inbox@gmail.com
Well you just sort of, you’re walking around like a zombie and you’re like sort of you can’t join in with things, I wouldn’t be talking to you like what I’m talking now. I know I might seem a bit high, but when you’re on [the antipsychotic drug] you can’t even be bothered holding a conversation you know, you’re just sat there saying yes or no. (p. 1317)

Although specific side effects are clearly highly individual and none are universal, it is undeniable that the general patterns described above, further substantiated by existing research on the role of striatal dopamine, extend far beyond “sedation” or “sleepiness.” Energy, motivation, pleasure, and “clear” thinking are unambiguously of enormous importance with respect to individuals’ pursuit of such goals as finishing school, finding (and keeping) a job, and engaging socially with family and friends. Indeed, the importance of such factors is underscored by the well-established disproportionate impact of the negative symptoms of schizophrenia—including amotivation, anhedonia, and energia—on real-world outcomes relative to positive symptoms.

Although the negative impacts of perceived dysphoric side effects on medication adherence are relatively well documented (e.g., Naber, Karow, & Lambert, 2005; Perkins, 2002), their influence on the therapeutic alliance as well as the potentially moderating role of clinician responses and attitudes have not been empirically investigated. In a suggestive qualitative investigation of psychopharmacology consultations in the UK, Seale, Chaplin, Lelliott, and Quirk (2007) identified a pronounced disconnect between patients’ and clinicians’ interpretation and estimation of the relevance and importance of experiences of “sedation” and “mental clouding.” Thus the researchers noted that prescribing psychiatrists often downplayed, positively re-framed, or reattributed complaints of excessive sleepiness or lack of drive to other factors. Although unremarked, the transcripts presented demonstrate not even a single instance in which the clinicians in question actually affirmed the medical legitimacy of their patients’ experiences, nor made any attempt to better understand their full reach and functional impact. Bringing two and two together, participants in a series of consumer focus groups I recently facilitated frequently remarked on their negative perceptions of prescribers’ seeming unwillingness to validate their experiences of psychotropic dysphoria, leading, at least in some cases, to dishonesty, nonadherence, and even total disengagement. Although the side effects themselves are clearly a problem, that is, negative prescriber attitudes attitudes may be the straw that breaks the camel’s back.

The science is there. “Neuroleptic dysphoria” is real and its effects are potentially far-reaching, at least for susceptible individuals. Isn’t it time to start validating patients’ experiences in the clinic as well as the laboratory?

REFERENCES


atractiva Scandinavica, 111, 29–34.


cation, sedation and mental clouding: An observational study of psychiatric consultations. Social Science & Medicine, 65(4), 698–711.


