Motivational drive and alprazolam misuse : a recipe for aggression?

ALBRECHT, Bonnie, STAIGER, Petra K., HALL, Kate, KAMBOUROPOULOS, Nicolas and BEST, David <http://orcid.org/0000-0002-6792-916X>

Motivational drive and alprazolam misuse: A recipe for aggression?

Short title

Drive, alprazolam and aggression

Authors

Bonnie Albrecht[a], Petra K. Staiger[a*], Kate Hall[a,b], Nicolas Kambouropoulos[a], & David Best[c]

Affiliations

[a]School of Psychology, Deakin University, Victoria, Australia

[b]Youth Substance and Advocacy Service, Victoria, Australia

[c]Sheffield Hallam University, Sheffield, United Kingdom

Word count (exc. abstract, tables, figures, references): 5090 (Abstract: 200)

*** corresponding author:** Petra K. Staiger – petra.staiger@deakin.edu.au; School of Psychology, Deakin University, 221 Burwood Highway, Burwood, VIC 3125. (P: +61 3 924 46876)

Date of Manuscript: 14 December 2015

Abstract

Benzodiazepine-related aggression is understudied in the literature, in particular little is known about the motivational factors which may contribute to the development of this paradoxical response. The revised Reinforcement Sensitivity Theory provides a theoretical framework from which to understand the relevant underlying motivational processes. The current study aimed to identify the role of approach and avoidance motivational tendencies in the occurrence of benzodiazepine-related aggression. Data regarding benzodiazepine and other substance use, approach and avoidance motivation, and general and physical aggressive behaviour were collected via self-report questionnaires. Participants were a convenience sample (n = 204) who reported using benzodiazepines in the previous year. Participants were primarily male (62.7%), aged 18-51 years old. Hierarchical multiple regressions indicated that general and physical aggression were predicted by alprazolam use and Drive, a facet of approach motivation. Overall, lower diazepam use significantly predicted higher levels of general aggression. However, when diazepam-preferring participants were examined in isolation of the larger sample (23.5% of sample), problematic (dependent) diazepam use was associated with greater aggression scores, as was dependence risk for alprazolam-preferring participants (39.7% of sample). The findings highlight the importance of motivational factors and benzodiazepine use patterns in understanding benzodiazepine-related aggression, with implications for violent offender rehabilitation.

Keywords: benzodiazepines, aggressive behaviour, Reinforcement Sensitivity Theory

Motivational drive and alprazolam use: A recipe for aggression?

1.0 Introduction

Benzodiazepines are commonly used to manage anxiety or agitated behaviour (Ashton, 2002). However, for an estimated 1-20% of users, benzodiazepine use is followed by an aggressive response (Lader, 2011). The somewhat paradoxical nature of this response, coupled with the high medical, financial and personal costs associated with aggressive behaviour, suggests that changes to prescribing policies and regulatory strategies may be required to reduce the likelihood of benzodiazepine-related aggression from occurring. However, surprisingly little attention has been paid to understanding the psychological processes associated with benzodiazepine-related aggression. Controlled laboratory studies have demonstrated that alprazolam and diazepam use can result in an increased aggressive response in some participants (e.g., Bond and Silveira, 1993; Bond et al., 1995; Ben-Porath and Taylor, 2002; Wallace and Taylor, 2009), and animal studies report the possible influence of concurrent alcohol use (de Almeida et al., 2010) and pre-existing aggressive tendencies (Ferrari et al., 1997; Weerts et al., 2010) in benzodiazepine-related aggression. Yet, few human studies have examined potential contributory factors (i.e., dose, other substance use, psychological or intrapersonal factors, situation; see Albrecht et al., 2014, for systematic review). Of note, irrespective of a long-standing proposal that intrapersonal factors are important in understanding this response (Lion et al., 1975; Hoaken and Stewart, 2003), only a handful of studies have investigated the role of various personality characteristics in benzodiazepine-related aggression (i.e., trait anxiety, hostility; Wilkinson, 1985; Cherek et al., 1990; Ben-Porath and Taylor, 2002; Dåderman et al., 2002). This limited research, and the absence of a clear theoretical framework with which to explore benzodiazepine-related aggression impacts on our ability to develop meaningful, and testable, hypotheses and intervention strategies. We argue that current models of approach and

avoidance motivational tendencies may be able to inform our understanding of benzodiazepine-related aggression.

Motivational systems are theorised to underlie a number of human behaviours, including violent and aggressive behaviour. Gray's (1982) Reinforcement Sensitivity Theory and its recent revision (rRST; Gray and McNaughton, 2003) purports to explain behavioural output and emotional expression based on three separate but interacting motivational systems. The behavioural approach system (BAS) promotes movement towards incentives and rewards, often involving goal-directed behaviour and impulsive action. The fight-flight-freeze system (FFFS) promotes fearful avoidance of a threat, and over-activation clinically presents as phobia or panic (Corr and Perkins, 2006). The behavioural inhibition system (BIS) promotes risk assessment and conflict resolution (Corr, 2008), and is stimulated by simultaneous and similar activation of the other two systems (Pickering and Corr, 2008). As demonstrated by prior research, the independent and interactive effects of these motivational systems have informed our understanding of aggressive behaviour. It is therefore expected that the application of this theory to benzodiazepine-related aggression will provide meaningful insight into the response, on which intervention strategies could be based.

Aggression appears to involve a strong approach motivational component (i.e., BAS mediated action such as antagonism; Smits and Kuppens, 2005). That is, aggression may in part be the result of high levels of motivated action towards goals or rewards. Indeed, studies with university students have reported that high levels of BAS are associated with anger and aggressive behaviour (Harmon-Jones, 2003; Harmon-Jones and Peterson, 2008). However, theoretical understanding of approach motivation (BAS) suggests that it involves multiple aspects, including behavioural restraint, planning and goal-directed behaviour (Segarra et al., 2014), and the use of a broad, unidimensional measure of BAS in the above studies fails to account for such complexity. Instead, greater specificity is afforded through the use of a

multidimensional measure of approach motivation. The BIS/BAS scales (Carver and White, 1994) were designed to account for the dynamic and multifaceted nature of the BAS.

Empirical evidence suggests that Drive is the most important facet of BAS in our understanding of aggressive behaviour (e.g., Seibert et al., 2010). Drive (BAS-Dr) involves persistent goal pursuit and functional impulsivity; whilst Fun Seeking involves dysfunctional impulsivity, with minimal thought to consequences; and Reward Responsiveness involves positive energy and affect in response to reward cues (Tull et al., 2010). BAS-Dr has been positively associated with the experience of anger (Harmon-Jones, 2003; Smits and Kuppens, 2005; Cooper et al., 2008), anger arousal, displaced aggression, the tendency to not suppress angry feelings or prevent the expression of anger (Cooper et al., 2008), self-reported physical aggression (Harmon-Jones, 2003), relational aggression (Miller et al., 2012), and laboratory proxies of aggressive behaviour (Seibert et al., 2010). In addition, Beaver and colleagues (2008) identified that with increasing BAS-Dr, neural structures and dopaminergic pathways are activated in a similar pattern to that observed in relation to both reward processing and aggression, providing some explanation as to why BAS-Dr is so important in understanding aggression. Further conceptual understanding of the link between BAS-Dr and aggressive behaviour is afforded through the concept of frustrative non-reward, which is experienced when the expected reward is higher than the actual reward (Corr, 2002). Indeed, although predominantly associated with the experience of positive affect (i.e., through goal attainment), BAS-Dr has also been associated with the experience of negative affect, especially sadness, frustration and anger, experienced in the context of blocked or challenged reward attainment (Carver, 2004). Such scenarios may influence an aggressive response. Following such theorising, aggression may be especially likely if the individual also experiences sensitivity to cues of punishment or threat (i.e., avoidance motivational tendencies). Essentially, aggressive behaviour may involve a facilitative interplay between

appetitive and aversive motivational systems, where aggression is more likely when an individual with high BAS-Dr also experiences strong avoidance tendencies.

Such an interaction may be especially important in the understanding of benzodiazepine-related aggression. Evidence suggests that benzodiazepines selectively interfere with the conflict resolution system (BIS) by making approach behaviour more likely (Pickering and Corr, 2008). As part of its conflict resolution role, the BIS mediates cautious approach behaviour when it is considered necessary to approach a threat (Perkins et al., 2007). In an individual with strong approach motivation tendencies (i.e., BAS-Dr), BIS may become increasingly activated in the context of threat or frustration compared to FFFS (i.e., goal frustrations/threats may be more likely to be considered necessary to approach rather than avoid in order to attain the goal). When coupled with benzodiazepine use, which further disinhibits the BIS from promoting risk averse avoidance behaviour, aggressive behaviour may result. Indeed, BIS has been associated with reactive aggression (Miller et al., 2012), potentially reflecting the frustration response, and at extremely high levels of BIS activation, the related emotional disturbance may increase aggression risk (Hatfield and Dula, 2014). As yet no studies have attempted to explore these specific hypotheses in substance-related aggression, particularly benzodiazepine-related aggression. Such investigation of the rRST motivational systems and their interactive effects will provide further insight into this relationship, with implications for violent offender rehabilitation and the continued prescription of benzodiazepines.

1.1 The current study

The current study aims to test the hypothesis that BAS-Dr plays a role in predicting benzodiazepine-related aggression, but that the interaction between BAS-Dr and BIS accounts for greater variance. Due to their prevalent use within the sample, the current study will explicitly focus on diazepam and alprazolam in relation to both general aggressive

behaviour (i.e., anger, hostility, verbal aggression) and specifically physical aggression. Data regarding the participants' substance use, mental health, and criminal history, and recent psychological functioning will also be gathered. It is predicted that:

1. BAS-Dr, or the tendency to persistently pursue appetitive goals, will significantly predict benzodiazepine-related general and physical aggression.
2. BAS-Dr will moderate the relationship between BIS and aggressive outcomes. Specifically, it is predicted that the relationship between BIS and benzodiazepine-related aggressive behaviour will be stronger for individuals with high levels of BAS-Dr.

2.0 Method

2.1 Design and procedure

Participants were recruited via a purposeful sampling method, which utilised an online electronic questionnaire and paper based questionnaires located at health services. Online participants were recruited through electronic platforms (Facebook, Reddit), newspaper adverts, and paper flyers posted around the host university. Health service clients were recruited from a community based outpatient alcohol and drug treatment service and a residential alcohol and drug treatment facility via flyers or conversation with their treating clinician. Consent was implied by completion of the questionnaire and all survey responses were anonymous. After completing the questionnaire, participants were invited to enter a separate draw for one of six $50.00 shopping vouchers and to provide feedback about the survey. The raffle was drawn at the completion of data collection. Inclusion criteria were age of 18 years or older and use of benzodiazepines in the past 12 months (whether prescribed or non-prescribed). There were no additional exclusion criteria. The study was approved by the relevant ethics committees.

2.2 Materials

2.2.1 Demographics

Demographic questions included current prescription medication, treatment history for drug, alcohol, and mental health issues, and history of substance-related or violent charges or convictions. A brief measure of recent psychological functioning (Depression, Anxiety and Stress Scales [DASS-21]; Lovibond and Lovibond, 1995) was also included.

2.2.2 Substance and benzodiazepine use

A modified version of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), an eight-item questionnaire designed to detect psychoactive substance use and related problems (WHO ASSIST Working Group [WHO], 2002), was used to assess lifetime substance involvement and benzodiazepine-related dependency and harms. The majority of the items were altered to refer only to the benzodiazepine the respondent selected as their preferred type for non-medically prescribed use. *Non-medically prescribed use* (NMP) was defined as using benzodiazepines not prescribed by their doctor or when taken more frequently or at higher doses than their doctor prescribed. Taking benzodiazepines for NMP reasons may include to feel better, get high, have fun, or to substitute a usual drug of choice. By separating medically-prescribed and NMP use, we were able to isolate data regarding the misuse of benzodiazepines, and specifically explore aggressive responses following such use. We focussed on non-medically prescribed use in order to further our understanding of the sequelae of benzodiazepine use which may not be readily observed or monitored by prescribers or other health professionals (e.g., due to the frequent diversion of benzodiazepines onto the black market; Best et al., 2013). Additional items regarding benzodiazepine and substance use patterns were developed through consultation with academics and clinicians within the alcohol and other drugs field, specifically regarding item wording, relevance and exhaustiveness. Respondents were instructed to select the most appropriate answer/s or provide brief written responses.

2.2.3 BIS/BAS

The Behavioural Inhibition System and Behavioural Activation System Scales (BIS/BAS; Carver and White, 1994) is a 24-item self-report questionnaire designed to assess Gray's (1982) reward and punishment sensitivities. Items are rated on a 4-point Likert scale (1 = strongly agree, 4 = strongly disagree), with four filler items. A five factor model was used to reflect the revised theory; the three BAS factors, BIS, and FFFS (Heym et al., 2008). In the current study, moderate to high internal consistency was demonstrated for each subscale ($\alpha = 0.67 - 0.82$).

2.2.4 Aggression

The Aggression Questionnaire (AQ; Buss and Perry, 1992) is a 29-item self-report questionnaire which measures physical aggression, verbal aggression, anger, and hostility. Items are rated on a 5-point Likert scale (1 = extremely uncharacteristic of me, 5 = extremely characteristic of me), and a total aggression score can be calculated by summing all subscale scores. The instructions were altered to prompt participants to respond to the questionnaire in relation to the last time they had used benzodiazepines for NMP reasons, on an occasion when they were not consuming other drugs or alcohol. Internal consistency for the current study was high for the total score ($\alpha = 0.95$) and across all factors ($\alpha = 0.84$-0.88).

2.3 Statistical analyses

Where possible, parametric analyses were conducted, and means, standard deviations, and 95% confidence intervals (CI) are reported. Non-parametric chi-square tests of independence are used where assumptions are violated and with categorical variables. Hierarchical multiple regressions were used to investigate the primary research questions.

2.3.1 Model specification and invariance testing

Model specification was purely conceptual, and based on understandings of the aggression and rRST literature. Therefore, age, gender, previous drug and alcohol use, and prior violent convictions were statistically controlled. However, due to the use of two

recruitment methods, it was necessary to determine whether the data could be pooled without deleterious effects on the main analyses. As determined through exploration of the larger sample, the internet and health centre recruitment subsamples differed on a number of demographic variables. Therefore, invariance analyses using the Chow test (DeMaris, 2004) were conducted, at the $p < 0.05$ standard. Based on the outcome of these tests, the prediction of both general aggression ($\Delta\chi^2$ (15) = 9310.373, $p < 0.05$) and physical aggression ($\Delta\chi^2$ (15) = 1368.56, $p < 0.05$) varied according to whether the data was pooled or separated by recruitment source. However, due to the size of the health centre subsample relevant for the aggression analyses (i.e., NMP use with AQ scores; $n = 30$), it is likely that the lack of power in the health centre subsample may have artificially led to a significant difference from the pooled sample model. The planned model on such a small subsample would likely inflate the chance of Type 2 error, due to the lack of statistical power available. An a priori *G*Power* (version 3.1.9.2) analysis indicated that a sample of 160 participants was required to run the planned model in order to detect a small effect (0.15) against the $p<0.05$ criterion. It was therefore decided to pool the data and include a sample recruitment variable in the analyses.

3.0 Results

3.1 Participant characteristics

The final sample consisted of 204 adult community members (62.7% male) who regularly use benzodiazepines, recruited via the internet ($n = 174$; 63.2% male) and health services ($n = 30$; 60.0% male), aged between 18 and 51 years old ($M = 27.12$, $SD = 8.21$). Participant demographic characteristics are displayed in Table 1.

The sample reported moderate to high scores across the BIS/BAS scales, and moderate levels of psychological distress (see Table 2). The sample reported high rates of poly-substance use, with the two most commonly used substances in the month prior to reporting (other than tobacco) being alcohol and cannabis (see Table 1). Less than a third of

the sample admitted previously injecting an illicit substance (*n* = 61; 29.9%), though almost half of these participants had done so in the last three months (*n* = 27; 44.26%). In the three months prior to survey completion, half (54.4%) of the sample reported drinking alcohol on at least a weekly basis, whilst 82.4% reported using illicit drugs on at least a weekly basis. Of these, the majority reported using one or two types of illicit drugs per week (77.4%), with 17.9% using three types, and only 4.8% (*n* = 8) using 4 or more types of illicit drugs per week.

3.1.2 Benzodiazepine profile

On average, participants began using NMP benzodiazepines at 20.46 years old (*SD* = 6.17). NMP benzodiazepines were most frequently acquired through friends (53.4%) or the black market (34.3%), and only 13.7% reported to have engaged in doctor shopping. Most participants (72.5%) reported using benzodiazepines with other substances; especially alcohol (17.6%), cannabis (11.3%), or both (8.3%). As expected, diazepam and alprazolam were most likely to be used for NMP reasons (52.9% and 54.3% respectively; see Table 3), and were explicitly preferred for NMP use by 23.5% and 39.7%, respectively. ASSIST scores generally reflected a moderate risk of dependence (see Table 2). Although used relatively infrequently over the year prior to survey completion (Table 3), participants consumed diazepam and alprazolam at high average doses (see Table 4). Alprazolam was used at the highest average doses, and at a level considerably higher than recognised prescribing guidelines[1] (i.e., up to 33mgs; 'Alprazolam', 2013). Diazepam and alprazolam were mostly used to reduce anxiety and tension (29.8%, 30.0% respectively) or to get high (14.5%, 24.6% respectively), as well as to reduce withdrawal from other substances (11.3%) for diazepam and to assist sleep (8.5%) for alprazolam.

3.2 Main analyses

[1] Prescribing guidelines suggest a daily range of 0.5-4.0mg per day ('Alprazolam', 2013).

Due to their high rate of misuse in the current sample (52.9-54.3%; see Table 3) compared to other benzodiazepines enquired about (9.3-24.6%), the role of diazepam and alprazolam were specifically assessed in the main analyses. It is notable that such patterns of use aligns with Australian data showing alprazolam and diazepam to be among the most widely prescribed (Islam et al., 2014) and misused (Nielsen et al., 2008; Stafford & Burns, 2012) benzodiazepines, and also the most widely studied in relation to exploring the benzodiazepine-aggression link (Albrecht et al., 2014).

Bivariate correlations between the variables of interest demonstrated that both general and physical aggression scores were significantly associated with higher risk of alprazolam and diazepam dependence, psychological distress (DASS), BAS-Drive, and having a violent conviction (see Table 5). Physical aggression was also positively associated with having a substance-related conviction. Increased alprazolam doses were significantly associated, albeit at a low strength, with weaker BIS-related anxiety and fear, having a substance-related conviction, and a tendency to use multiple other substances when consuming benzodiazepines. Higher diazepam doses were associated with having violent and substance-related convictions. Increased risk of dependence to alprazolam and diazepam was associated with increased psychological distress, though alprazolam risk was not associated with DASS-anxiety.

3.2.1 Predicting benzodiazepine-related aggression

Two hierarchical multiple regressions were conducted, to explore whether BIS/BAS variables could predict benzodiazepine-related aggression over and above control and benzodiazepine variables. In both models, control variables were entered at Step 1, diazepam and alprazolam use at Step 2, BIS/BAS main effects at Step 3, and the interaction term at Step 4. Two cases were removed for the purposes of the subsequent analyses due to violation of regression assumptions. The variables used to compose the interaction term (BAS-Dr, BIS-

Anx) were centered in order to reduce multicollinearity, and categorical variables included in the regression analyses were standardized using dummy-coding.

3.2.1.1 General aggression. Inclusion of the control variables at Step 1 explained 5.5% of the variance in general aggression (F_{change} (6, 195) = 1.903, p = 0.082). Entry of the benzodiazepine variables at Step 2 significantly improved the model, explaining an additional 3.7% of the variance; F_{change} (2, 193) = 3.910, p = 0.022. Entry of the BIS/BAS main effects at Step 3 again significantly improved the model, explaining an additional 6.7% of the variance; F_{change} (5, 188) = 3.009, p = 0.012. The inclusion of the interaction term at Step 4 did not significantly improve the model (ΔR^2 = 0.008); F_{change} (1, 187) = 1.769, p = 0.185. However, the final model, with all the variables in the equation, was significant and accounted for 16.7% of the total variance in general aggression; F(14, 187) = 2.682, p = 0.001. Alprazolam and diazepam use, and BAS-Dr significantly attributed unique variance to general aggression, whilst recruitment group and BAS-FS approached significance (see Table 6). Inspection of the data indicates that BAS-Dr and alprazolam use made the strongest unique contributions to general aggression. Combined, BAS-Dr (5.29%) and alprazolam use (4.04%) contributed just under 10.0% towards the explanation of variance in general aggression, as calculated from the part correlation coefficients (Pallant, 2007).

Due to the significant findings pertaining to diazepam and alprazolam, it was explored whether general aggression differed according to benzodiazepine dose. Two follow-up independent samples t-tests (two-tailed) indicated that levels of general aggression did not differ between those using alprazolam within the prescribing range or above (t(116) = -1.054, p = 0.294, 95% C.I. = -13.52 to 4.13, Cohen's d = -0.20), or between those using diazepam within the prescribing range or above; t(108) = -0.849, p = 0.398, 95% C.I. = -14.25 to 5.71, Cohen's d = -0.18.

3.2.1.2 Physical aggression. Inclusion of the control variables at Step 1 explained 6.4% of the variance in physical aggression. Entry of the benzodiazepine variables at Step 2 did not significantly improve the model ($\Delta R^2 = 0.015$); F_{change} (2, 193) = 1.542, $p = 0.217$. Entry of the BIS/BAS variables at Step 3 significantly improved the model ($\Delta R^2 = 0.057$); F_{change} (5, 188) = 2.459, $p = 0.035$. The inclusion of the interaction term at Step 4 did not significantly improve the model ($\Delta R^2 = .000$); F_{change} (1, 187) = 0.000, $p = 0.991$. The final model accounted for 13.5% of the total variance in physical aggression; $F(14, 187) = 2.084$, $p = 0.014$. Alprazolam and BAS-Dr significantly attributed unique variance to physical aggression, although recruitment group and BAS-FS approached significance (see Table 7). BAS-Dr (4.6%) and alprazolam use (1.8%) uniquely contributed a combined 6.4% towards the explanation of variance in physical aggression.

A follow-up independent samples t-test (two-tailed) indicated that levels of physical aggression did not differ between those using alprazolam within the prescribing range or above ($t(116) = -1.658$, $p = 0.100$, 95% C.I. = -5.36 to 0.48, Cohen's $d = -0.31$).

4.0 Discussion

Benzodiazepine-related aggression is poorly understood. The current study aimed to explore the role of approach and avoidance motivational tendencies in benzodiazepine-related aggression. It was proposed that BAS-Dr specifically would be important in understanding this response, but that the interaction between BAS-Dr and BIS would account for greater variance in benzodiazepine-related aggression. The data partially supported these predictions, however the moderation effect was not observed.

4.1 The role of BAS-Dr in benzodiazepine-related aggression

The tendency to pursue appetitive goals in a persistent manner (BAS-Dr) has been consistently associated with aggression and related tendencies (i.e., anger; Cooper et al., 2008; Seibert et al., 2010; Miller et al., 2012). The current study extends this literature, by

hypothesising that BAS-Dr is important in benzodiazepine-related aggression. In support of this hypothesis, BAS-Dr was the strongest unique predictor of both general aggression and physical aggression, over and above the influence of benzodiazepine type (diazepam and alprazolam). Such outcomes align with research indicating the importance of BAS-Dr in the prediction of aggressive behaviour compared to other intrapersonal factors (Seibert et al., 2010), and importantly, support the contention that our understanding of benzodiazepine-related aggression may be enhanced via recourse to intrapersonal differences (Lion et al., 1975; Hoaken and Stewart, 2003).

Individuals with strong BAS-Dr have been described as antagonistic, competitive, and willing to work hard to achieve goals, even if at the expense of others (Segarra et al., 2014). Such individuals hold high expectations of rewards following goal attainment (Harmon-Jones, 2003) and their experienced affect is strongly reflective of their perceived progress towards their goal (Carver, 2004). For example, in the context of challenged or blocked goal attainment, individuals with high BAS-Dr may experience frustration or anger (Carver, 2004), such as frustrative non-reward (Corr, 2002). Aggressive behaviour then becomes increasingly likely, as during frustration, such individuals display reduced impulse control (Beaver et al., 2008) and attention to risk or punishment cues (Avila, 2001). Their ability to respond appropriately to stressors or frustrations may become further disinhibited in the context of benzodiazepine use (Paton, 2002). Indeed, the current data indicate that individuals with stronger BAS-Dr tendencies experienced greater anxiety and stress, which may reflect difficulty attaining desired outcomes (Carver, 2004), and tended to consume benzodiazepines in the context of other substances, which may further impact on their coping or self-regulation ability. However, the absence of appropriate causal testing limits the conclusions drawn from such associations, though the findings do clearly support the role of persistent action towards desired goals in benzodiazepine-related aggressive behaviour. As such,

prescribers may benefit from exploring patients' ability to engage in effective impulse control and frustration tolerance strategies prior to prescribing benzodiazepines. Clinical presentations which involve established dysregulation of approach and avoidance motivational systems (such as post-traumatic stress disorder) may also warrant additional caution when prescribing benzodiazepines (e.g., Guina et al., 2015). Investigation of the benzodiazepine-aggression relationship within such clinical samples is therefore highlighted.

The findings have implications for the design of rehabilitation interventions for individuals who engage in substance-related aggression. The rRST clearly elucidates that different motivational tendencies are associated with different neural structures and patterns of activation, and therefore differentially impact other intrapersonal characteristics such as emotional tendencies and expression, learning processes, and personality (Corr, 2009). Specifically, approach motivations are primarily associated with dopaminergic pathways (Pickering and Corr, 2008), and increasing BAS-Dr activation has been associated with increased activation of the amygdala (emotional processing centre) and dopamine pathways, as well as blunted activation of other neural structures, in patterns synonymous with those implicated in aggression and reward processing (Beaver et al., 2008). The implication of BAS-Dr in benzodiazepine-related aggression suggests that such substance-related aggression is not altogether dissimilar to non-substance-related aggression, with clear ramifications for the treatment of individuals who engage in aggression or violence following benzodiazepine use. Notably, although benzodiazepine use may increase the likelihood of disinhibition and aggression, removal of the associated substance in isolation of interventions targeting the underlying motivational factors (and the related emotional and information processing factors, such as expectations regarding aggression; Anderson and Bushman, 2002) may be unlikely to result in effective desistance from aggressive behaviour. Such a conclusion is further suggested by our findings that BAS-Dr attributed more variance to both aggression

outcomes than did either benzodiazepine type tested. It is noted that such theorising is made in the absence of structural and/or functional imaging data.

Interestingly, the expected moderation effect between a strong appetitive and strong aversive motivational system on benzodiazepine-related aggressive behaviour failed to significantly influence either aggression model. Given that our sample displayed only moderate levels of aggression, the proposed interactive effect may be more likely in a more violent sample, against clearly defined violent incidents. Furthermore, aggression risk may be associated with extremely high levels of BIS activation (Hatfield and Dula, 2014), whilst our sample displayed only moderately-high BIS activation. The moderating effect may therefore only be relevant to investigations of benzodiazepine-related aggression in individuals with higher levels or approach and avoidance motivations than those observed in the current sample.

4.2 Role of benzodiazepine type in benzodiazepine-related aggression

The primary aim of the current study was to explore the role of approach and avoidance motivational tendencies in order to better understand benzodiazepine-related aggression. This was done with specific consideration of two commonly used benzodiazepines, diazepam and alprazolam. Notably, our findings suggest that alprazolam poses a greater risk than diazepam for subsequent aggressive behaviour, supporting prior discussions which have described alprazolam as one of the most problematic benzodiazepines (Horyniak et al., 2012; Rintoul et al., 2013), and its recent up-scheduling to a controlled substance within Australia. However, as alluded to above, consideration of alprazolam use in isolation of other contributing factors fails to adequately account for the processes underlying aggressive behaviour. Indeed, Lion and colleagues' (1975) highlighted that it is the interaction between benzodiazepine use, the situation, and intrapersonal factors (and not the benzodiazepine alone) which influences subsequent aggressive behaviour. Given its short

acting effects, association with poly-substance use in the current sample, and the common goal to become intoxicated (25.6%), alprazolam-related aggression may indeed reflect the context of use, to a greater extent than the physiological effects of alprazolam. However, further research using urinalysis and an in-depth analysis of substance use patterns is required.

Interestingly, general aggression was significantly negatively predicted by diazepam use. Within the current sample, diazepam was used more for alleviation of negative emotional and physical states (i.e., anxiety, tension, or effects of withdrawal; 41.1%), rather than to get high (14.5%), whereas alprazolam use is more evenly attributed to both reasons. This differentiation further highlights the role that approach motivations (rather than avoidance motivational tendencies) may have in the experience of benzodiazepine-related aggression. Furthermore, unlike alprazolam, diazepam appears to be infrequently used within the context of poly-substance use, and therefore may be generally used in scenarios with less risk of aggressive interactions. In addition, only when diazepam-preferring participants were examined in isolation, of whom predominantly displayed a moderate or high risk of dependence (i.e., difficulty managing diazepam use, experience of problematic diazepam-related outcomes), did we find a positive association with aggressive outcomes. Comparatively, the regression analyses were conducted with all participants who had reported historically using diazepam for NMP reasons (i.e., not necessarily frequent, ongoing, dependent use). Therefore, it could be concluded that diazepam poses a risk for benzodiazepine-related aggression only in those who display increasingly problematic patterns of diazepam use, rather than to the majority who use diazepam on a less regular basis. This has important implications for the continued prescription of diazepam, highlighting the importance of prescribers carefully monitoring patient adherence to low dose, short term use, and the potential benefits of prioritising non-medicinal approaches when

assisting patients (Dobbin, 2014; Lader, 2014). Comparatively, alprazolam appears to be a risk for aggression at both dependent (problematic) levels and for those with less frequent use, and may be best prescribed only after exhausting other treatment options.

4.3 Limitations and strengths

A number of limitations must be acknowledged. Due to the cross-sectional nature of the study, causality cannot be implied, and data collection relied on uncorroborated, retrospective self-report which may be vulnerable to attributional and self-presentational biases and memory decay. The likelihood of selection bias impacting the sample is also taken into account, as is the absence of a non-benzodiazepine using control group. In addition, the findings are limited in generality, and cannot be reliably applied to individuals who commit more severe violence. Moreover, it cannot be discounted that other substances used in combination with benzodiazepines may have impacted the findings (Sweeney and Payne, 2012). Furthermore, the current study did not permit direct examination of frustrative non-reward or neural activity, as this can only be examined when reward pathways are activated.

Despite these caveats, the current study has a number of important and unique strengths. First, specific benzodiazepines are explored, allowing greater specificity than the majority of cross-sectional studies available. Second, the sample is relatively large, with an almost even gender split; the latter feature absent in a number of well-designed, though male-only, examinations of benzodiazepine-related aggression (see Albrecht et al., 2014 for a review). Third, the response is explored through the application of a clear theoretical framework.

5.0 Conclusion

Intrapersonal factors are important in understanding benzodiazepine-related aggression (Lion et al., 1975; Hoaken and Stewart, 2003). Notably, individuals exhibiting high BAS-Dr may be more vulnerable to engaging in aggression post-benzodiazepine use. In

addition, general diazepam use (i.e., not in the context of dependency) appears to reduce the risk of general aggressive behaviour (i.e., anger, hostility, verbal aggression), whilst alprazolam increases the risk of aggression, regardless of dose. The findings highlight the benefit of attending to approach and avoidance motivations, as well as frustration tolerance and impulse control, within offender rehabilitation programs and when prescribing benzodiazepines. Importantly, this study supports current guidelines which emphasise exploring (and exhausting) non-medicinal options before prescribing benzodiazepines, and the rescheduling of alprazolam to a controlled substance.

Acknowledgements

The authors are extremely grateful for the assistance of Debbie Becker during the recruitment stage of this study and to the participants for completing the survey.

Funding: No funding was sought for this specific paper.

Declarations of interest

We declare that none of the authors are in receipt of financial support, or have any relationship that may pose a conflict in relation to the content presented in the submitted manuscript.

Contributors

All authors contributed to questionnaire development. BA and PS developed the study rationale. Data cleaning, statistical analysis, and original draft manuscript completed by BA. All authors contributed to the editing of the manuscript.

References

Albrecht, B., Staiger, P.K, Hall, K., Miller, P., Best, D., Lubman, D. I., 2014. Benzodiazepine use and aggressive behaviour: a systematic review. Australian and New Zealand Journal of Psychiatry 48(12), 1096-1114.

Alprazolam, September, 2013. In MIMS. Retrieved from www.mims.com.au.

Anderson, C. A., Bushman, B. J., 2002. Human aggression. Annual Review of Psychology 53(1), 27-51.

Avila,C., 2001. Distinguishing BIS-mediated and BAS-mediated disinhibition mechanisms: a comparison of disinhibition models of Gray (1981, 1987) and of Patterson and Newman (1993). Journal of Personality and Social Psychology 80(2), 311-324.

Beaver, J. D., Lawrence, A. D., Passamonti, L., Calder, A. J., 2008.Appetitive motivation predicts the neural response to facial signals of aggression. The Journal of Neuroscience 28(11), 2719-2725.

Ben-Porath, D. D., Taylor, S. P., 2002. The effects of diazepam (Valium) and aggressive disposition on human aggression: an experimental investigation. Addictive Behaviors 27(2), 167-177.

Best, D., Wilson, A., Reed, M., Lloyd, B., Eade, A., Lubman, D. I., 2013. Alprazolam and wider benzodiazepine misuse in Australia – sources of supply and evidence of harms. Australian and New Zealand Journal of Psychiatry 47, 94-95.

Bond, A. J., Curran, H. V., Bruce, M. S., O'Sullivan, G., 1995. Behavioural aggression in panic disorder after 9 weeks' treatment with alprazolam. Journal of Affective Disorders 35(3), 117-123.

Bond, A. J., Silveira, J. C., 1993. The combination of alprazolam and alcohol on behavioral aggression. Journal of Studies on Alcohol 54(5), 30-39.

Buss, A. H., Perry, M. P., 1992. The Aggression Questionnaire. Journal of Personality and Social Psychology 63, 452-459.

Carver, C. S. (2004). Negative affects deriving from the behavioral approach system. Emption, 4(1), 3-22. doi: 10.1037/1528-3542.4.1.3

Carver, C. S., White, T. L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. Journal of Personality & Social Psychology 67(2), 319-333.

Cherek, D. R., Steinberg, J. L., Kelly, T. H., Robinson, D. E., Spiga, R., 1990. Effects of acute administration of diazepam and d-amphetamine on aggressive and escape responding of normal male subjects. Psychopharmacology 100, 173-181.

Cooper, A., Gomez, R., Buck, E., 2008. The relationships between the BIS and BAS, anger and responses to anger. Personality and Individual Differences 44, 403-413.

Corr, P. J., 2002. J. A. Gray's reinforcement sensitivity theory and frustrative nonreward: a theoretical note on expectancies in reactions to rewarding stimuli. Personality and Individual Differences 32, 1247-1253.

Corr, P. J. (Ed.), 2008. The reinforcement sensitivity theory of personality. Cambridge University Press, Cambridge.

Corr, P. J., 2009. The reinforcement sensitivity theory of personality, in: Corr, P. J., Matthews, G. (Eds.), The Cambridge handbook of personality psychology. Cambridge University Press, Cambridge, pp. 347-376.

Corr, P. J., Perkins, A. M., (2006. The role of theory in the psychophysiology of personality: From Ivan Pavlov to Jeffrey Gray. International Journal of Psychophysiology 62, 367-376.

Dåderman, A. M., Fredriksson, B., Kristiansson, M., Nilsson, L. H., Lidberg, L., 2002. Violent behavior, impulsive decision-making, and anterograde amnesia while

intoxicated with flunitrazepam and alcohol or other drugs: a case study in forensic psychiatric patients. The Journal of the American Academy of Psychiatry and the Law 30(2), 238-251.

de Almeida, R. M. M., Saft, D. M., Rosa, M. M., Miczek, K. A., 2010. Flunitrazepam in combination with alcohol engenders high levels of aggression in mice and rats. Pharmacology, Biochemistry & Behavior 95(3), 292-297.

DeMaris, A., 2004. Regression with social data: Modeling continuous and limited response variables. John Wiley & Sons, New Jersey.

Dobbin, M., 2014. Pharmaceutical drug misuse in Australia. Australian Prescriber 37(3), 79-81.

Farinde, A., May, 2014. Benzodiazepine equivalency table. Retrieved from http://emedicine.medscape.com/article/2172250-overview

Ferrari, P. F., Parmigiani, S., Rodgers, R. J., Palanza, P., 1997. Differential effects of chlordiazepoxide on aggressive behavior in male mice: the influence of social factors. Psychopharmacology 134(3), 258-266.

Gray, J. A., 1982. The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system, Oxford University Press, Oxford.

Gray, J. A., 1994. Three fundamental emotion systems, in Ekman, P., Davidson, R. J. (Eds.), The nature of emotion: Fundamental questions. Oxford University Press, New York, pp. 243–247.

Gray J. A., McNaughton, N., 2003. The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system. Oxford University Press, New York.

Guina, J., Rossetter, S.R., DeRhodes, B.J., Nahhas, R.W., Welton, R.S., 2015. Benzodiazepines for PTSD: a systematic review and meta-analysis. Journal of Psychiatric Practice 21(3), 281-303.

Harmon-Jones, E., 2003. Anger and the behavioral approach system. Personality and Individual Differences 35, 995-1005.

Harmon-Jones, E., Peterson, C. K., 2008. Effect of trait and state approach motivation on aggressive inclinations. Journal of Research in Personality 42, 1381-1385.

Hatfield, J., Dula, C. S., 2014. Impulsivity and physical aggression: examining the moderating role of anxiety. American Journal of Psychology 127(2), 233-243.

Heym, N., Ferguson, E., Lawrence, C., 2008. An evaluation of the relationship between Gray's revised RST and Eysenck's PEN: distinguishing BIS and FFFS in Carver and White's BIS/BAS scales. Personality and Individual Differences 45(8), 709-715.

Hoaken, P. N. S., Stewart, S. H., 2003. Drugs of abuse and the elicitation of human aggressive behaviour. Addictive Behaviors 28(9), 1533-1554.

Horyniak, D., Reddel, S., Quinn, B., Dietze, P., 2012. The use of alprazolam by people who inject drugs in Melbourne, Australia. Drug & Alcohol Review 31(4), 585-590.

Islam, M. M., Conigrave, K. ., Day, C. A., Nguyen, Y., Haber, P. S., 2014. Twenty-year trends in benzodiazepine dispensing in the Australian population. Internal Medicine Journal 44(1), 57-64.

Jones, S. E., Miller, J. D., Lynam, D. R., 2011. Personality, antisocial behavior, and aggression: a meta-analytic review. Journal of Criminal Justice 39, 329-337.

Lader, M., 2011. Benzodiazepines revisited – will we ever learn? Addiction 106(12), 2086-2109.

Lader, M., 2014. Benzodiazepine harm: how can it be reduced? British Journal of Clinical Pharmacology 77(2), 295-301.

Lion, J. R., Azcarate, C. L., Koepke, H. H., 1975. "Paradoxical rage reactions" during psychotropic medication. Diseases of the Nervous System 36(10), 557-558.

Lovibond, S. H., Lovibond, P. F., 1995. Manual for the depression anxiety stress scales, second ed. Psychology Foundation of Australia, Sydney.

Miller, J. D., Zeichner, A., Wilson, L. F., 2012. Personality correlates of aggression: Evidence from measures of the five-factor model, UPPS model of impulsivity, and BIS/BAS. Journal of Interpersonal Violence 27(14), 2903-2919.

Nielsen, S., Bruno, R., Carruthers, S., Fischer, J., Lintzeris, N., Stoove, M., 2008. Investigation of pharmaceutical misuse amongst drug treatment clients. Turning Point Alcohol and Drug Centre Inc., Melbourne. Pallant, J., 2007. SPSS survival manual, third ed. Allen & Unwin, NSW.

Perkins, A. M., Kemp, S. E., Corr, P. J., 2007. Fear and anxiety as separable emotions: an investigation of the revised reinforcement sensitivity theory of personality. Emotion *7*(2), 252-261.

Pickering, A., Corr, P., 2008. J. A. Gray's reinforcement sensitivity theory (RST) of personality, in Boyle, G. E., Matthews, G., Saklofske, D. H. (Eds.), Personality theories and models, volume one. SAGE Publications, London, pp. 239-256.

Rintoul, A. C., Dobbin, M. D. H., Neilsen, S., Degenhardt, L., Drummer, O. H., 2013. Recent increase in detection of alprazolam in Victorian heroin-related deaths. Medical Journal of Australia 198(4), 2069-209.

Segarra, P., Poy, R., López, R., Moltó, J., 2014. Characterizing Carver and White's BIS/BAS subscales using the five factor model of personality. Personality and Individual Differences 61-62, 18-23.

Seibert, L. A., Miller, J. D., Pryor, L. R., Reidy, D. E., Zeichner, A., 2010. Personality and laboratory-based aggression: comparing the predictive power of the five-factor model, BIS/BAS, and impulsivity across context. Journal of Research in Personality 44, 13-21.

Smits, D. J. M., Kuppens, P., 2005. The relations between anger, coping with anger, and aggression, and the BIS/BAS system. Personality and Individual Differences 39, 783-793.

Stafford, J., Burns, L., 2012. Findings from the Illicit Drug Reporting System (IDRS) (Australian drug trends series no. 73). National Drug and Alcohol Research Center, University of New South Wales, Sydney.

Sweeney, J., Payne, J., 2012. Drug use monitoring in Australia: 2009-10 report on drug use among police detainees (AIC Monitoring Reports No. 17). Australian Institute of Criminology, Canberra.

Tull, M. T., Gratz, K. L., Latzman, R. D., Kimbrel, N. A., Lejuez, C. W., 2010. Reinforcement sensitivity theory and emotion regulation difficulties: a multimodal investigation. Personality and Individual Differences 49, 989-994.

Wallace, P. S., Taylor, S. P., 2009. Reduction of appeasement-related affect as a concomitant of diazepam-induced aggression: evidence for a link between aggression and the expression of self-conscious emotions. Aggressive Behavior 35(2), 203-212.

Weerts, E. M., Miller, L. G., Hood, K. E., Miczek, K. A., 1992. Increased GABA-a dependent chloride uptake in mice selectively bred for low aggressive behaviour. Psychopharmacology 108(1-2), 196-204.

Wilkinson, C. J., 1985. Effects of diazepam (Valium) and trait anxiety on human physical aggression and emotional state. Journal of Behavioral Medicine 8(1), 101-114.

WHO ASSIST Working Group, 2002. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): development, reliability, and feasibility. Addiction 97(9), 1183-1194.

Tables

Table 1. *Participant demographic characteristics.*

Characteristic	Total	
	N	%
Male	128	62.7
Female	76	37.3
Country of Origin		
Australia	74	36.3
New Zealand	5	2.5
Asia	6	2.9
Europe	13	6.4
USA/Canada	96	47.1
United Kingdom	8	3.9
Other	2	1.0
Student		
Yes	89	43.6
No	112	54.9
Education		
Before year 12	31	15.2
Year 12	79	38.7
University/TAFE	94	46.1
Employed		
No	100	49.0
Yes	100	49.0
Treatment	Ever	Current
Drug	86 (42.2)	42 (20.6)
Alcohol	31 (15.2)	23 (11.3)
Mental Health	140 (68.6)	83 (40.7)
Criminal History	Ever charged	Ever convict
AOD	66 (32.4)	39 (19.1)
Violence	16 (7.8)	10 (4.9)
Substance Use	Lifetime	Month prior
Tobacco	183 (89.7)	124 (60.8)
Alcohol	194 (95.1)	156 (76.5)
Cannabis	189 (92.6)	121 (59.3)
Cocaine	122 (59.8)	27 (13.2)
Amphetamines	168 (82.4)	76 (37.3)
Inhalants	67 (32.8)	15 (7.4)
Hallucinogens	143 (70.1)	41 (20.1)

Opioids	148 (72.5)	85 (41.7)

Note. Unless where specified, sample percentages are enclosed in brackets. Substance use frequencies reflect any use (illicit or prescribed).
Note. AOD = Alcohol and other drugs; convict = convicted.

Table 2. *Standardised questionnaire score ranges, means and standard deviations.*

Tool	Total		
	Range	*M (n)*	*SD (%)*
ASSIST			
SSI diazepam (*n* = 45)	2-36	12.76	10.20
Low risk	0-3	(9)	(20.0)
Moderate risk	4-26	(30)	(66.7)
High risk	27+	(6)	(13.3)
SSI alprazolam (*n* = 77)	0-39	15.74	11.22
Low risk	0-3	(8)	(10.4)
Moderate risk	4-26	(52)	(67.5)
High risk	27+	(17)	(22.1)
DASS-21			
Depression	0-21	10.12	6.44
Anxiety	0-21	7.78	5.57
Stress	0-21	10.01	5.38
BIS/BAS			
BAS-Dr	5-16	10.66	2.47
BAS-FS	6-16	12.11	2.37
BAS-RR	11-20	15.99	2.11
BIS-Anx	6-16	13.09	2.41
BIS-Fear	4-12	9.21	2.08
AQ			
Total score	29-137	69.99	23.90
Physical	9-43	19.06	7.91

Note. ASSIST = Alcohol, Smoking and Substance Involvement Screening Test (WHO, 2002); AQ = Aggression Questionnaire (Buss & Perry, 1992); BIS/BAS = Behavioural Inhibition System and Behavioural Activation System Scales (Carver & White, 1994); BAS-Dr = Drive, BAS-RR = Reward Responsiveness; BAS-FS =Fun Seeking; BIS-Anx = Anxiety; DASS-21 = Depression, Anxiety, and Stress Scales (Lovibond & Lovibond, 1995); SSI = Specific Substance Involvement score.

Table 3. *Lifetime NMP use per benzodiazepines, frequency of alprazolam and diazepam use in past year*.

Benzodiazepine	Ever NMP *n* (%)		Frequency of use	
			Alprazolam[a]	Diazepam[a]
Alprazolam	157 (54.3)	Never	33 (20.2)	36 (22.0)
Temazepam	61 (21.2)	Once or twice	49 (30.1)	61 (37.2)
Oxazepam	39 (13.5)	Monthly	30 (18.4)	28 (17.1)
Lorazepam	71 (24.6)	Weekly	32 (19.6)	14 (8.5)
Diazepam	153 (52.9)	Daily	19 (11.7)	25 (15.2)
Clonazepam	70 (24.2)			
Flunitrazepam	27 (9.3)			

[a] Percentages reflect those reporting ever using selected benzodiazepine for NMP reasons.

Table 4. *Typical and maximum alprazolam and diazepam doses used per day, with approximate diazepam equivalent doses (DZM).*

Benzodiazepine	Typical				Maximum			
	n	Range	*M (SD)*	Approximate DZM[a] (mgs)	*n*	Range	*M (SD)*	Approximate DZM (mgs)
Alprazolam	119	0-15.0	3.88 (4.29)	38.8	118	0-33.0	8.12 (8.71)	81.2
Diazepam	111	0-61.0	16.96 (15.71)	16.96	110	1-161.0	39.81 (41.97)	39.81

Note. Approximate DZM = approximate diazepam equivalent dose; mgs = milligrams.
[a] Approximate DZM computed using a 1:10 ratio for alprazolam, as suggested by dosing conversion table outlined by Farinde (2014).

Table 6. *Hierarchical multiple regression predicting benzodiazepine-related general aggression*.

	B	*S.E*	Beta	*t*	*p*	95% C.I. for *B*		Part correlation coefficient
						Lower	Upper	
Constant	91.56	20.09		4.558	0.000	51.93	131.19	
Recruitment	8.96	4.10	0.15	1.793	0.075	-0.90	18.82	0.120
Age	-0.06	0.20	-0.03	-0.316	0.752	-0.45	0.33	-0.021
Gender	-1.13	3.42	-0.02	-0.331	0.741	-7.88	5.62	-0.022
Viol Conv	10.09	7.82	0.10	1.290	0.199	-5.34	25.52	0.086
Reg Dr	-2.42	4.71	-0.04	-0.513	0.609	-11.70	6.87	-0.034
Reg Alc	2.12	3.89	0.05	0.545	0.586	-5.55	9.80	0.036
Alprazolam	11.70	3.88	0.25	3.012	**0.003**	4.04	19.36	0.201
Diazepam	-8.83	3.73	-0.19	-2.366	**0.019**	-16.19	-1.47	-0.158
BAS-FS	-0.166	0.87	-0.17	-1.905	0.058	-3.38	0.06	-0.127
BAS-RR	-0.76	0.90	-0.07	-0.849	0.397	-2.53	1.01	-0.057
BAS-Dr^	2.86	0.83	0.30	3.451	**0.001**	1.23	4.50	0.230
BIS-Anx^	0.10	0.83	0.01	0.124	0.901	-1.54	1.74	0.008
BIS-Fear	1.03	0.98	0.09	1.056	0.293	-0.90	2.97	0.070
AnxXDr ^	0.35	0.26	0.09	1.330	0.185	-0.17	0.86	0.089

Note. Viol Conv = violent conviction; Reg Drg = regular drug use (previous 3 months); Reg Alc = regular alcohol use (previous 3 months); BAS-Dr = drive subscale, BAS-RR = reward responsiveness subscale; BAS-FS = fun seeking subscale; BIS-Anx = anxiety subscale; BIS-Fear = fear subscale; AnxXDr = interaction term. ^ centered variables.

Table 7. *Hierarchical multiple regression predicting benzodiazepine-related physical aggression*.

	B	*S.E*	Beta	*t*	*p*	95% C.I. of *B*		Part correlation coefficient
						Lower	Upper	
Constant	29.51	6.79		4.349	0.000	16.12	42.89	
Recruitment	3.15	1.69	0.16	1.867	0.063	-0.18	6.48	0.127
Age	-0.02	0.07	-0.03	-0.319	0.750	-0.15	0.11	-0.022
Gender	-0.46	1.16	-0.03	-0.397	0.692	-2.74	1.82	-0.027
Viol Conv	3.79	2.64	0.11	1.434	0.153	-1.42	9.00	0.098
Reg Drg	-0.06	1.59	-0.00	-0.037	0.971	-3.20	3.08	-0.003
Reg Alc	0.86	1.31	0.06	0.654	0.514	-1.73	3.45	0.044
Alprazolam	2.63	1.31	0.17	2.004	**0.046**	0.04	5.22	0.136
Diazepam	-1.95	1.26	-0.12	-1.546	0.124	-4.44	0.54	-0.105
BAS-FS	-0.58	0.29	-0.18	-1.96	0.052	-1.16	0.01	-0.133
BAS-RR	-0.19	0.30	-0.05	-0.613	0.541	-0.78	0.41	-0.042
BAS-Dr^	0.88	0.28	0.28	3.154	**0.002**	0.33	1.44	0.215
BIS-Anx^	-0.12	0.28	-0.03	-0.419	0.676	-0.67	0.44	-0.028
BIS-Fear	-0.16	0.33	-0.04	-0.47	0.639	-0.81	0.50	-0.032
AnxXDr ^	0.00	0.09	0.00	0.011	0.991	-0.17	0.17	0.001

Note. Viol Conv = violent conviction; Reg Drg = regular drug use (previous 3 months); Reg Alc = regular alcohol use (previous 3 months); BAS-Dr = drive subscale, BAS-RR = reward responsiveness subscale; BAS-FS = fun seeking subscale; BIS-Anx = anxiety subscale; BIS-Fear = fear subscale; AnxXDr = interaction term. ^ centered variables.

Table 5. *Bivariate correlations between factors of interest*.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1. Age	-																				
2. Gender	0.21 **																				
3. Alp dose typical	0.25 **	0.01																			
4. Alp dose maximum	0.13	-0.04	0.91 **																		
5. Dz dose typical	0.02	-0.07	0.35 **	0.40 **																	
6. Dz dose maximum	-0.04	-0.07	0.29 *	0.37 **	0.83 **																
7. DASS Dep	0.08	0.01	0.08	0.10	0.08	0.05															
8. DASS Anx	0.04	0.09	-0.12	-0.13	0.16	0.09	0.58 **														
9. DASS Str	0.11	0.11	-0.03	-0.05	0.15	0.09	0.66 **	0.80 **													
10. BAS DR	0.06	0.05	0.08	0.11	0.12	0.11	0.03	0.24 **	0.23 **												
11. BAS FS	0.00	-0.06	0.08	0.18	0.04	0.11	0.08	0.07	0.03	0.48 **											
12. BAS RR	0.00	0.07	0.05	0.07	0.03	-0.02	-0.16 *	0.00	0.03	0.40 **	0.38 **										

13. BIS Anx	0.04	0.13	-0.25**	-0.28**	-0.06	-0.14	0.24**	0.29**	0.36**	-0.17**	-0.19*	0.11									
14. BIS Fear	-0.01	0.08	-0.21*	-0.25**	0.05	-0.12	0.30**	0.30**	0.36**	-0.24**	-0.32**	-0.00	0.54**								
15. AQ Total	0.04	-0.03	0.09	0.08	0.14	0.17	0.33**	0.33**	0.46**	0.21**	-0.01	0.05	0.08	0.08							
16. AQ Phys	0.04	-0.06	0.10	0.10	0.14	0.16	0.22**	0.22**	0.34**	0.22**	0.03	0.05	-0.04	-0.07	0.87**						
17. Viol Conv	0.10	-0.03	0.07	0.14	0.16	0.40**	0.04	0.12	0.15*	0.28**	0.18**	0.08	-0.05	-0.23**	0.17*	0.21**					
18. AOD Conv	0.25**	-0.06	0.24**	0.28**	0.19	0.30**	0.05	0.11	0.04	0.13	0.14*	0.04	-0.11	-0.15*	0.05	0.14*	0.35**				
19. Poly BZD	-0.04	-0.07	0.25**	0.25**	0.15	0.03	0.10	0.15*	0.14*	0.22**	0.25**	0.14*	-0.02	-0.05	0.13	0.12	0.14*	0.05			
20. ASSIST Alp	0.24*	-0.17	0.38**	0.41**	0.50**	0.50**	0.27*	0.17	0.31**	0.16	0.04	-0.01	0.02	-0.12	0.33**	0.28*	0.21	0.30**	0.24*		
21.ASSIST Dz	0.33*	0.28	-0.18	-0.22	0.39*	0.46**	0.30*	0.43**	0.54**	0.28	-0.05	0.05	0.25	0.07	0.53**	0.48**	0.26	0.13	0.11	a	
22. Reg Sub	-0.07	-0.02	0.18	0.13	0.02	-0.06	0.15	0.05	0.10	0.12	0.21**	0.02	-0.15	-0.10	0.14	0.14	0.03	0.13	0.22**	0.23	-0.14

Note. Alp = alprazolam; Dz = diazepam; DASS Dep = DASS Depression scale; DASS Anx = DASS Anxiety scale; DASS Str = DASS Stress scale; BAS Dr = Drive scale; BAS FS = Fun Seeking scale; BAS RR = Reward Responsiveness scale; BIS Anx = Anxiety scale; BIS Fear = Fear scale; AQ = Aggression Questionnaire; AQ Phys = Aggression Questionnaire Physical subscale; Viol Conv = violent conviction; AOD Conv = drug or alcohol related conviction; Poly BZD = use of other substances when taking non-medically prescribed benzodiazepines; ASSIST Alp = total ASSIST score for those who prefer alprazolam; ASSIST Dz = total ASSIST score for those who prefer diazepam; Reg Sub = number of substances regularly (at least weekly) used.

[a] correlation unable to be computed as discrete subsamples based on preferential benzodiazepine used for non-medically prescribed reasons.

* $p < 0.01$

** $p < 0.001$