The Open Addiction Journal, **2014,** *7,* **17-21**

Prospective and Retrospective Memory Deficits Associated with Androgenic Anabolic Steroid Use

Thomas Heffernan* and Terence O'Neill

Collaboration for Alcohol and Drug Research (CDAR), Department of Psychology, Northumbria University, Newcastle upon Tyne, NE1 8ST, UK

Abstract: The recreational use of androgenic anabolic steroids (AAS) has been associated with a range of health and psychological problems in the past, but very little research has considered what impact AAS might have upon cognition and memory. The present study aimed to identify whether the recreational use of AAS is linked to deficits in everyday retrospective memory (RM) and everyday prospective memory (PM). We assessed self-reports of RM and PM in 25 regular AAS users and 28 Non-Users (all were males, regular gym users and aged between 18-30 years) using the Prospective and Retrospective Memory Questionnaire. A Recreational Drug Use Questionnaire was used to measure AAS use and alcohol use. The Hospital Anxiety and Depression Scale measuredtwo dimensions of mood (anxiety and depression). The results revealed thatrecreational AAS users reported significantly more everyday RM lapses (AAS Mean = 2.41 *vs* Non-Users Mean = 1.66; $p<0.001$)and significantly more everyday PM lapses (AAS Mean = 2.79 *vs* Non-User Mean = 1.84; $p<0.001$) than the Non-User group. These findings were not attributable to other substance use or mood variations. This is the first study to demonstrate everyday memory deficits associated with AAS use and it is suggested that such deficits be added to the growing list of health and cognitive problems associated with AAS use.

Keywords: Androgenic anabolic steroids, everyday memory, prospective memory, retrospective memory.

INTRODUCTION

Androgenic anabolic steroids (AAS) are a group of synthetically produced variants of the male sex hormone testosterone. They have traditionally been used clinically to treat a range of medical conditions, such as delayed puberty, loss of lean muscle mass, cancer and AIDS, but more recently have been used in a recreational sporting context to promote fat reduction and muscle building. Since the 1980s many millions of individuals worldwide have used AAS in a sporting context in order to promote muscle growth and improve athletic performance, with recent figures of AAS prevalence rates amongst gym users as high as 38% and a clear preponderance of male users [1-3]. Since the onset of recreational AAS use, research has shown that persistent use of such drugs is now associated with a number of health and psychiatric complications.

A myriad of health and psychiatric complications have been associated with the recreational use of AAS. For example, somatic complications such as physical skin lesions (including acne and abscesses), edema (swelling due to excess fluid being trapped, typically in the extremities of the body), and more severe symptoms including cardiac palpitations, long-term cardiovascular diseases (including cardiac dysrhythmia, myocardial infarction and pulmonary embolism), decreased fertility and sexual dysfunction [4-9]. In terms of psychiatric symptoms, AAS use has been associated with increased levels of aggression, including in some severe cases, increased hostility, antisocial and violent behaviour towards others – sometimes also referred to as "Roid Rage" [10-13]. AAS use has also been linked to severe mental disorders, including mania, depression, suicidality, psychoses and may be addictive [14-19]. However, it should be noted that the degree to which AAS users are at risk of such complications is dependent upon a range of factors, such as length of AAS use, dose, and the use of other drugs alongside AAS, for example excessive drinking can exacerbate such problems and act as a confound on the results.

Only a handful of studies to date have considered what effect recreational AAS use has on cognition, including memory function. In one study [20] 44 male non-users aged between 29-55 years were compared with a comparison group of 31 male participants who had used AAS in a recreational context for an average of seven years. Each participant was asked to complete five cognitive tests that assessed a wide range of cognitive functions: memory for shapes and locations of objects, memory for lists of words, reaction time, sustained attention, and speed of information processing. Results revealed that long-term AAS users performed significantly worse than non-users on visuospatial memory (the Pattern Recognition Memory test), with no differences detected on any of the other cognitive tests. Performance scores on the visuospatial memory task declined noticeably with increasing lifetime AAS dose and this finding remained stable after controlling for potential confounding factors, such as other substance use, indicating that the findings were likely to be attributable to AAS use. In a more recent study, 22 adult male AAS users were

*Address correspondence to this author at the Collaboration for Alcohol and Drug Research (CDAR), Department of Psychology, Northumbria University, Newcastle upon Tyne, NE1 8ST, UK; Tel: 0044191 227 4037; Fax: 0044191 227 3190; E-mail: tom.heffernan@northumbria.ac.uk

1874-9410/14

administered 4 computerized tests from the Cambridge Neuropsychological Test Automated Battery and the Iowa Gambling Task. Subsample analyses indicated that on-cycle users (those who used AAS with interspersed periods of abstinence) had reduced performance on cognitive measures of inhibitory control and attention, with no reduction in performance evident on tests of planning or decision making [21]. Taken together these findings suggest there may be selective cognitive deficits associated with persistent AAS use.

The deficits observed in the two previous studies [20, 21] are all examples of *retrospective memory* (RM) – which refers to the recall of information for people, words, numbers and events encountered or experienced in the past [22]. The first aim of the current study was therefore to assess whether AAS use impedes RM within an everyday context, beyond the laboratory based context used in the two previously published studies. The second aim of the current study was to extend our understanding of putative everyday memory deficits associated with AAS use by assessing everyday *prospective memory* (PM) – which refers to remembering a planned intention and action at an appropriate time in the future [22]. RM is thought to play a major role in prospective remembering [23], for example, RM helps to store the intended PM plan prior to its enactment and helps retrieve the content of the intention when the time for initiating the plan is reached. Therefore, since both RM and PM are intimately related, any deficits in RM associated with AAS use should be accompanied by deficits in PM. The overall objective of the current study was to assess putative deficits in everyday RM and PM associated with AAS use when compared with a Non-User comparison group. The Prospective and Retrospective Memory Questionnaire (PRMQ) [24] was used to measure self-reported everyday RM and PM lapses within an everyday context. The following hypothesis was tested: if regular use of AAS does compromise everyday memory then it is expected that the AAS user group should report more deficits in terms of RM and PM, when compared to a non-user group.

MATERIALS AND METHODOLOGY

Design and Setting

This study was conducted using a non-experimental design and was questionnaire based. Ethical clearance was granted by the School of Life Sciences at Northumbria University. Participation was voluntary and each participant was tested individually for approximately 15 minutes on campus.

Participants

An original sample of 300 undergraduate students studying at university in the North East of England was canvassed as a part of a general (unpublished) project on students' recreational drug use, mood and everyday memory. From this data base a group of AAS users and a comparison group of Non-Users were selected for the current study. The following exclusion criteria were used to determine the final sample included in the current study.1. Given that females rarely use AAS and that the majority of research on AAS use is based on male users [1], the current study focused on males only to reflect this pattern. 2. Since other drug use (such as excessive drinking, cannabis and ecstasy) have been linked to memory deficits independent of AAS use [25-27] anyone who reported having used one or more of these substances/drinking excessively was excluded from the final sample. 3. Anyone who reported using alcohol within the last 48 hours was also excluded in order to control for possible 'hangover' effects. 4. Anyone who reported having suffered/was currently suffering from a psychiatric condition (e.g. substance-dependence, clinical depression or amnesia) which might affect cognition independent of AAS use was also excluded from the final sample. 5. Finally, only participants aged between 18-30 years were included in the final sample in order to reduce any age-related memory effects. Given that mood has been known to affect everyday memory regardless of drug use [28, 29] this was analysed and compared between the two groups. Normal (non-excessive) alcohol use per week, last alcohol use in hours and the number of years spent drinking alcohol were also analysed and compared between the two groups. Based on these exclusion criteria, the original sample of 300 participants canvassed was reduced to 53, within which 25 were regular recreational AAS users and 28 were Non-Users. All were male, aged between 18-30 years and all were regular gym users. The AAS user group had a mean age of 23.8 (SD = 2.97), used AAS on average 2 times per week (SD = 0.57), with an average dose of 149 mg per occasion (SD = 132) and had last used AAS an average of 4.2 days prior to participation (SD = 5.76). The 28 who did not use AAS made up the Non-User group (Mean age = 22.3 (SD = 2.41)). All participants were unpaid volunteers who consented to participation and were debriefed.

Measures and Procedure

RM and PM were assessed using the Prospective and Retrospective Memory Questionnaire (PRMQ) which is a standardised self-report measure developed by previous researchers [24]. The PRMQ assesses self-reported RM and PM slips in everyday life and shows high internal consistency, with the reliability on Cronbach's alpha being 0.89. On the PRMQ, 8 items pertain to RM (e.g., "Do you repeat the same story to the same person on different occasions?") and 8 items pertain to PM (e.g., "Do you decide to do something in a few minutes' time and then forget to do it?"). Each participant rated how often they experienced such failures on a 5-point scale from "very often" (5) to "never" (1) by circling the response that best reflects their memory ability. A mean score for RM slips/failures was calculated, along with a mean score for PM slips/failures. A mean score for each scale (the RM and PM scales) was calculated by totalling the sum of scores on each scale and dividing this by the number of questions (8), with a higher score in both cases indicating more memory slips/failures. A modified version of a Recreational Drug Use Questionnaire (RDUQ) used in previous research [25-27] was used here to measure AAS use and alcohol indices – i.e. the number of units of alcohol used per week, when alcohol was last used in hours and the number of years spent drinking alcohol. [Since anyone who smoked, used an illegal substance (e.g. cannabis or ecstasy), drank excessively or had drunk alcohol within the past 48-hours, or had reported a psychiatric illness, was excluded prior to the study, these questions were omitted for the final 53

participants]. The Hospital Anxiety and Depression Scale (HADS) measured mood in terms of levels of anxiety and depression. HADS is a 14-item standardised self-report questionnaire; 7 items of which measured generalised anxiety symptoms and 7 generalised depressive symptoms; with the higher score indicating a greater frequency of anxiety or depression symptoms. The HADS has been shown to be a valid and reliable measure of mood in non-clinical samples [30]. All measures were collected by self-reports and no biological measures were taken. Each participant was tested individually and in a quiet location at the university. The order of presentation remained constant across participants, with the PRMQ administered first, and followed by the RDUQ and finally the HADS.

Data Analysis and Statistical Methods

All data was entered into SPSS-21. Since Shapiro-Wilk tests for normality revealed that the data for the self-reported RM and PM scores from PRMQ, thenumber of years spent drinking alcohol, last alcohol use in hours, HADS anxiety scores and HADS depression scores were not normally distributed, non-parametric Mann-Whitney U tests were performed on this data. Finally, since the Shapiro-Wilk tests for normality revealed the data for the number of units of alcohol consumed per week was normally distributed across the two groups, an independent t-test was applied to this data.

RESULTS

Table **1** below contains the mean scores and standard deviations (in brackets) comparing the AAS users with the Non-Users on the number of alcohol units consumed per week, the number of years spent drinking alcohol, last alcohol use in hours, HADS anxiety scores, HADS depression scores, and the mean scores for the RM and PM subscales of the PRMQ. Non-parametric Mann-Whitney U tests were performed to ascertain the presence of any significant differences between the AAS users and Non-Users. These tests revealed that AAS users reported significantly more self-reported failures in RM (U = 179.50, p<0.005) and PM (U = 163.50, p<0.001) when compared with the Non-Users. Mann-Whitney U tests revealed no significant differences between the AAS users and Non-Users in terms of years spent drinking alcohol (U = 45.50, p = 0.47), last alcohol use in hours (U = 31.00, p = 0.10), HADS anxiety (U = 243, p = 0.054), or HADS depression scores (U = 308.00, p = 0.46). Finally, an independent t-test revealed no significant difference between the two groups in terms of the number of units of alcohol consumed per week (t(22) = 21.88, p = 0.07).

Table 1. Descriptive data across AAS users AND Non-users.

	AAS Users (N = 25)	Non-Users (N = 28)
Alcohol Units Per week	22.3 (2.25)	17.2 (7.64)
Years Drinking Alcohol	7.00 (1.26)	7.05 (5.28)
Last Alcohol Use in Hours	76.0 (18.0)	88.0 (161)
HADS Anxiety	3.76 (1.94)	2.89 (2.67)
HADS Depression	7.44 (3.58)	7.75 (4.52)
RM*	2.41 (0.81)	1.66 (0.55)
PM*	2.79 (1.09)	1.84 (0.47)

Means and standard deviations (in brackets) comparing the AAS users with the Non-Users on the number of alcohol units consumed per week, the number of years spent drinking alcohol, their last alcohol use in hours, HADS anxiety scores, HADS depression scores, and the RM and PM mean scores from the PRMQ. An asterisk indicates a significant between-group difference at p < 0.005 or below.

DISCUSSION

The present study compared the recreational use of AAS in a sports context, comparing two groups of regular gym users –a group of AAS users and a Non-User comparison group on everyday RM and PM lapses. From a large sample size of 300 questioned originally about their general drug use, mood and everyday memory; after omitting anyone who reported drinking excessively or reported using alcohol within the past 24 hours, those who smoked, those who used illicit drugs, or those who suffered from a psychiatric disorder, the present study compared 25 regular recreational AAS users and 28 Non-Users, all of whom were regular gym users and male. The results from this sample revealed that the AAS user group reported significantly more RM and PM lapses in an everyday context compared with the Non-User group. The two groups did not differ significantly in terms of weekly (moderate) alcohol use, the total number of years spent drinking alcohol, last alcohol use in hours, or mood. Therefore the findings cannot be attributable to potentially confounding factors such as other drug use [25-27] or mood [28-30] known to affect memory independently. The finding that the recreational use of AAS leads to everyday memory problems, specifically RM and PM deficits, is generally consistent with previous work that has shown cognitive/ memory deficits associated with AAS use and it is suggested that RM and PM deficits be added to the growing list of cognitive deficits associated with AAS use. The finding that AAS use impedes everyday RM suggests that the memory deficits experienced by AAS users extends beyond the laboratory based context found in the two previously published pieces of research [20, 21]. The second finding that AAS use impedes PM extends our understanding further by suggesting users also have problems when it comes to planning for future actions. To our knowledge this analysis is the first study that has looked at AAS use within an everyday memory context and may be important due to the critical role RM and PM play in everyday independent living [31].

Given the scarcity of research into the cognitive deficits associated with AAS use, it is not surprising that relatively little is known about the exact mechanisms that may underpin the cognitive deficits found in previous studies. However, recent animal research [32] has provided evidence that supra-physiological doses of AAS can cause neurotropic unbalance and related behavioural disturbances in Nerve Growth Factor (NGF) levels and NGF receptor expression in the hippocampus and in the basal forebrain of the rats exposed to high doses of AAS. NGF mediates higher brain functions such as learning and memory and the findings from this work raises the concern that persistent AAS use in humans may affect those mechanisms that lie at the core of neuronal plasticity (the brain's ability to reorganize itself by forming new neural connections across a person's life-span). Given the importance of the basal forebrain in producing

acetylcholine which plays a key role in the ability of brain cells to transmit information to one another [33] and the role the hippocampus plays in memory consolidation [34], it is feasible that the memory deficits observed in previous work and in the current study may reflect damage caused to brain plasticity in humans who use AAS. However, further work on the potential interaction between persistent AAS use, brain plasticity and memory deficits in human populations is clearly needed before any firm conclusions can be reached. Taking into account the data from previous studies about the health, psychiatric and cognitive problems associated with AAS use, it is striking that despite these being widely publicised individuals continue to use the drug. It is important to attempt to ascertain why this might be the case and attempt to understand users' motivations. A more detailed examination using qualitative methods or open-ended questions may provide us with some insight into AAS users' perceptions of the benefits of use outweighing the costs [35]. Such an approach might also provide insights into whether they are aware of what impact AAS use has upon everyday cognition.

LIMITATIONS AND FUTURE DIRECTIONS

The present study is limited in a number of ways and these factors need to be considered when interpreting the findings reported here. First the sample mainly consists of students and it is likely that students will be of above average intelligence and well educated. It is therefore important to determine whether the same effects are found with wider populations within society. The reliability and validity of the verbal reports of drug use provided by participants could be explored further in future studies based on the use of biological assays (e.g., urinary or saliva samples) to verify each participant's drug use and to look at whether there is a relationship between AAS use and everyday memory deficits, a dose-related study. What impact the lifetime dose of AAS might have upon everyday memory should also be pursued in future research. On a similar note, although the PRMQ has been proven to be a valid and reliable measure of everyday RM and PM lapses which correlates with objective measure on these constructs [24] future research might wish to verify these deficits by using objective measures, such as the Doors and People test as a measure of RM and the Cambridge Prospective Memory Test as a measure of PM. Since RM and PM are closely linked to executive processes – a collection of processes responsible for multiple aspects of cognition, including planning, task coordination, impulse control, and attention [36], future work might wish to observe what impact persistent AAS use has upon all three sets of interrelated cognitive processes. Given the roles RM and PM play in everyday life and independent living [31] it is important to determine the degree to which persistent AAS use might impinge upon actual memory performance within a real world memory paradigm, since it is the real-world context that is likely to be most important to those affected. Finally, although the use of AAS is found predominantly in males, its impact on female cohorts is worthy of future consideration.

CONCLUSION

The overall objective of the study was to assess whether AAS use was associated with greater deficits in everyday RM and PM when compared with a Non-User comparison group. The findings support this contention by demonstrating significantly more RM and PM deficits in the AAS user group. This is the first study to observe an association between AAS use and everyday memory deficits, with the focus here on RM and PM. The results of our study are of relevance to policymakers, health care professionals, researchers and AAS user themselves, given that everyday memory processes such as RM and PM are seen as critical to independent living. For example, failures in recalling information from ones past or forgetting to complete future actions can seriously compromise everyday function. The use of AAS in a non-medical context has become major global health issue that requires further research and attention.

ACKNOWLEDGEMENTS

Dr. Heffernan and Dr. O'Neill both contributed equally to the design, analysis and composition of the manuscript and its final revisions.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

REFERENCES

[1] Kanayama G, Hudson J, Pope Jr HG. Illicit anabolic–androgenic steroid use. Horm Behav 2010; 58: 111-21.

[2] Skarberg K, Nyberg F, Engstrom I. Multisubstance use as a feature of addiction to anabolic-androgenic steroids. Eur Addict Res 2009; 15: 99-106.

[3] Thiblin I, Petersson A. Pharmacoepidemiology of anabolic androgenic steroids: A review. Fundam Clin Pharmacol 2005; 19: 27-44.

[4] D'Andrea A, Caso P, Salerno G, *et al*. Left ventricular early myocardial dysfunction after chronic misuse of anabolic-androgenic steroids: a Doppler myocardial and strain imaging analysis. Br J Sports Med 2007; 4: 149-155.

[5] Maravelias C, Dona A, Stefanidou M, Spiliopoulou C. Adverse effects of anabolic steroids in athletes: A constant threat. Toxicol Lett 2005; 158: 167-75.

[6] Melchert RB, Welder AA. Cardiovascular effects of androgenic-anabolic steroids. Med Sci Sports Exerc 1995; 27: 1252-62.

[7] Quaglio G, Fornasiero A, Mezzelani P, Moreschini S, Lugoboni F, Lechi A. Anabolic steroids: dependence and complications of chronic use. Intern Emerg Med 2009;4: 289-96.

[8] Sullivan ML, Martinez CM, Gennis P, Gallagher EJ. The cardiac toxicity of anabolic steroids. Prog Cardiovasc Dis 1998; 41: 1-15.

[9] Quaglio G, Fornasiero A, Mezzelani P, Moreschini S, Lugoboni F, Lechi A. Anabolic steroids: Dependence and complications of chronic use. Intern Emerg Med 2009;4: 289-296.

[10] Choi P, Parrott A, Cowan D. High-dose anabolic steroids in strength athletes: effects upon hostility and aggression. Hum Psychopharmacol 1990; 5: 349-56.

[11] Corrigan B. Anabolic steroids and the mind. Med J Aust 1996; 165: 222-6.

[12] Pagonis TA, Angelopoulos NV, Koukoulis GN, Hadjichristodoulou CS, Toli PN. Psychiatric and hostility factors related to use of anabolic steroids in monozygotic twins. Eur Psychiatry 2006; 21: 563-9.

[13] Thiblin I, Kristiansson R, Rajs J. Anabolic androgenic steroids and behavioural patterns among violent offenders. J Forensic Psychiat 1997; 8: 299-310.

[14] Brower K. Anabolic steroids: Addictive, psychiatric and medical consequences. Am J Addic 1992; 1(2): 100-14.

[15] Center for Substance Abuse Treatment. *Substance abuse treatment advisory. Anabol steroids* 2006; 5(3): 1-4.
[16] Hall RC, Hall RC. Abuse of supra physiologic doses of anabolic steroids. South Med J 2005; 98(5): 550-55.
[17] Perry PJ, Yates WR, Andersen KH. Psychiatric symptoms associated with anabolic steroids: a controlled, retrospective study. Ann Clin Psychiatry 1990; 2(1): 11-17.
[18] Pope HG, Katz DL. Psychiatric and medical effects of anabolic-androgenic steroid use: a controlled study of 160 athletes. Arch Gen Psychiatry 1994; 51(5): 375-82.
[19] Talih F, Fattal O, Malone D. Anabolic steroid abuse: psychiatric and physical costs. Cleve Clin J Med 2007; 74(5): 341-52.
[20] Kanayama G, Kean J, Hudson JI, Pope HG. Cognitive deficits in long-term anabolic-androgenic steroid users. Drug Alcohol Depend 2013; 130(1): 208-14.
[21] Hildebrandt T, Langenbucher JW, Flores A, Harty S, Berlin H. The Influence of Age of Onset and Acute Anabolic Steroid Exposure on Cognitive Performance, Impulsivity, and Aggression in Men. Psychol Addict Behav 2014.
[22] Baddeley AD, Eysenck M, Anderson MC, Eds. Memory. Hove: Psychology Press 2009.
[23] McDaniel MA, Einstein GO, Eds. Prospective memory: An overview and synthesis of an emerging field. UK: Sage 2007.
[24] Smith G, Del Sala S, Logie RH, Maylor EA. Prospective and retrospective memory in normal ageing and dementia: A questionnaire study. Memory 2000; 8: 311-321.
[25] Heffernan TM. The impact of excessive alcohol use on prospective memory: A brief review. Curr Drug Abuse Rev 2008; 1: 36-41.
[26] Rodgers J, Buchanan T, Scholey AB, Heffernan TM, Ling J, Parrott AC. Patterns of drug use and the influence of gender on self-reports of memory ability amongst ecstasy users: A web based study. J Psychopharmacol 2003; 17:379-386.
[27] Heffernan TM, O'Neill T, Moss M. Smoking and everyday prospective memory: A comparison of self-report and objective methodologies. Drug Alcohol Depend 2010; 112: 234-8.
[28] Cuttler C, Graf P. Sub-clinical compulsive checkers show impaired performance on habitual, event- and time-cued episodic prospective memory tasks. J Anxiety Disord 2009; 23: 813-23.
[29] Parrott AC, Morinan A, Moss M, Scholey A. Understanding Drugs and Behaviour. Chichester, UK: Wiley 2004.
[30] Snaith RP, Zigmond AS. Hospital anxiety and depression scale. Windsor, NFER: Nelson 1994.
[31] Brandimonte MA, Einstein GO, McDaniel MA, Eds. Prospective memory: Theory and applications (Chap 5). UK: Psychology Press 2014.
[32] Pieretti S, Mastriota M, Tucci P, *et al*. Brain nerve growth factor unbalance induced by anabolic androgenic steroids in rats. Med Science Sports Exercise 2013; 45(1): 29-35.
[33] Sharma R, Engemann S, Sahota P, Thakkar MM. Role of adenosine and wake‐promoting basal forebrain in insomnia and associated sleep disruptions caused by ethanol dependence. J Neurochem 2010; 115(3): 782-94.
[34] Deng W, Aimone JB, Gage FH. New neurons and new memories: How does adult hippocampal neurogenesis affect learning and memory? Nat Rev Neurosci 2010; 11(5): 339-50.
[35] Bahrke MS, Yesalis CE, Kopstein AN, Stephens JA. Risk factors associated with anabolic-androgenic steroid use among adolescents. Sports Med 2000; 29(6): 397-405.
[36] Kliegel M, McDaniel MA, Einstein GO, Eds. Prospective Memory: Cognitive, Neuroscience, Developmental and Applied Perspectives. pp. 283-302. New York: Lawrence Erlbaum Associates 2008.

Received: July 30, 2014 Revised: October 2, 2014 Accepted: October 12, 2014