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Anabolic androgenic steroid dependence is associated with executive dysfunction

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ABSTRACT

Background: Anabolic androgenic steroid (AAS) dependence is associated with a high prevalence of intra- and interpersonal problems, hence it is central to identify cognitive factors related to the development and maintenance of dependence.

Methods: The study explores executive functions (EFs) in a sample of 174 male weightlifters, divided into three groups; 1) AAS dependents; n = 58, 2) AAS non-dependents; n = 38 and 3) AAS non-users; n = 78, using a targeted battery of neuropsychological (NP) tests, and self-report questionnaires assessing EFs in everyday life, ADHD symptoms and psychological distress.

Results: Multivariate analysis of variance showed significant between-group differences on several EFs, including working memory [$F(2, 169) = 13.79$, $p < .001$, $\eta p^2 = 0.14$], mental flexibility [$F(2, 169) = 4.82$, $p = .009$, $\eta p^2 = 0.05$], problem-solving [$F(2, 169) = 4.77$ $p = .010$, $\eta p^2 = 0.05$] and inhibition [$F(2, 163) = 4.15$, $p = .017$, $\eta p^2 = 0.05$]. Additionally, significant between-group differences were seen for self-reported problems with EFs [$F(2, 124) = 4.38$ $p = .015$, $\eta p^2 = 0.07$], ADHD symptoms [$F(2, 124) = 7.02$ $p = .001$, $\eta p^2 = 0.10$], and psychological distress [$F(2, 124) = 4.11$ $p = .019$, $\eta p^2 = 0.06$]. Post hoc tests showed that AAS dependents exhibited poorer EFs and reported more psychological distress compared to non-users.

Conclusion: AAS dependence is associated with executive dysfunction, which might be related to continued abuse despite adverse side-effects and social consequences. Increased awareness of executive dysfunction could have important implications for treatment and rehabilitation.

1. Introduction

1.1. Anabolic androgenic steroids

Illicit use of anabolic androgenic steroids (AAS) is considered to be a growing public health problem throughout the Western world (Kanayama et al., 2008). AAS comprise testosterone and a large category of synthetic relatives and is commonly taken in doses 10–100 times greater than the natural male production (Brower, 2002). The administration pattern of AAS varies; some use the compounds in cycles of 6–18 weeks, with drug-free periods in between in order to restore the suppressed hypothalamic-pituitary-gonadal (HPG) axis. In drug-free periods many users experience withdrawal symptoms like depression, irritability, anxiety, fatigue and insomnia (Maravelias et al., 2005). To avoid this, many users administer AAS continuously in a pattern called "cruise and blast", where they alternate between periods with low and high doses. AAS is associated with a wide range of adverse effects, both physical and psychiatric (Kanayama et al., 2008; Oberlander and Henderson, 2012; Pope Jr et al., 2013), in addition to maladaptive behavior (Hall et al., 2005; Hallgren et al., 2015; Kanayama et al., 2010; Miller et al., 2005). The side-effects are idiosyncratic as some experience few whereas others experience severe consequences, but the risk of adverse side-effects seems to increase with the duration of AAS use (Pope Jr et al., 2013). Around 30 percent of AAS users develop a dependency syndrome, characterized by withdrawal symptoms and continued use despite adverse side-effects and negative impact on social relations (Kanayama et al., 2009a). The mechanisms underlying AAS dependence is not fully understood, although it seems that AAS dependence share several elements with other drug dependencies (Nyberg and Hallberg, 2012; Wood, 2008), including subtle brain structure

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Table 1
Demographics and other clinical characteristics.

	Non-users (n = 78)	Non-dependent (n = 38)	Dependent (n = 58)	Main effect of group		
Variable	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	*F*	*p-value*	ηp^2
Age (years)	36.5 (8.8)	38.3 (11.6)	38.7 (9.5)	.97	.380	.01
Height (cm)	179.9 (13.3)	183.7 (5.8)	180.1 (6.9)	2.0	.136	.02
Weight (kg)	92.6 (11.2)	97.2 (10.5)	100.2 (17.7)	5.5	.005[a]	.06
Education (years)	16.4 (2.5)	15.7 (2.5)	13.9 (1.9)	20.4	< .001[ab]	.19
IQ	115.5 (11.3)	111.5 (10.3)	105.4 (9.7)	15.2	< .001[ab]	.15
AAS use		Mean (*SD*)	Mean (*SD*)	*t*	*p-value*	*d*
Debut age		24.6 (8.9)	20.9 (4.8)	2.41	.019	.63
Estimated weekly dose		692.0 (536.6)	1196.9 (664.8)	−4.15	< .001	.84
Total years of use		6.4 (4.5)	13.3 (6.8)	−6.04	< .001	1.37

Bonferroni post hoc test: a = AAS dependents significantly different from non-users and b = AAS dependents significantly different from AAS non-dependents.

abnormalities (Hauger et al., 2019b). Compared with non-using peers, AAS users have more hospital admissions and higher risk for premature death (Horwitz et al., 2019; Petersson et al., 2006). It seems that the AAS dependent users account for the majority of the public health problems posed by AAS use (Kanayama et al., 2008, 2009c). Thus, it is very important to identify cognitive factors influencing decision making strategies related to the development and maintenance of dependence.

1.2. Testosterone and cognition

AAS easily pass the blood-brain barrier and readily affect the central nervous system (CNS) (Banks, 2012). Androgen receptors (AR) are widely expressed in the CNS, not least in regions such as the amygdala, hippocampus, hypothalamus, brain stem and cerebral cortex (Simerly et al., 1990), implicated in a wide range of functions. It appear to be a parabolic association between testosterone levels and brain health, where testosterone in physiological doses can have neuroprotective effects (Hammond et al., 2001), but supra-physiological doses on the other hand can be neurotoxic (Pomara et al., 2015). A similar association between testosterone and cognitive functions is supported by studies demonstrating that testosterone levels at the tails of the distribution are associated with impaired cognitive function (Magnusson et al., 2009; McGinty et al., 2014; Wallin and Wood, 2015; Warren et al., 2008). Recently, it has been demonstrated that long-term AAS users perform poorer on different cognitive tasks (Bjørnebekk et al., 2019; Kanayama et al., 2013), and self-report more prospective memory lapses and executive function deficits (Heffernan et al., 2015), compared to non-using weightlifters.

1.3. Executive functions

Executive functions (EFs) can be defined as several cognitive control mechanisms mediating the ability to successfully regulate thoughts, emotions and behaviors in a goal directed manner. Although the definitions vary, most agree that EFs should be viewed as a multi-faceted construct that consists of several sub-functions, such as behavioral inhibition, interference control, working memory and mental flexibility (Diamond, 2013; Miyake and Friedman, 2012). Even though the sub-functions are partly distinct, they interrelate flexibly in response to complex cognitive demands (Miyake et al., 2000). EFs are essential for mental and physical health and adaptive social functioning. Executive dysfunction is associated with several disorders, including attention-deficit/hyperactive disorder (ADHD) (Willcutt et al., 2005) and substance-use disorder (SUD) (Diamond, 2013). Numerous studies report associations between substance abuse and impaired EFs (Fernandez-Serrano et al., 2010; Lundqvist, 2005; Verdejo-García and Pérez-García, 2007), and alterations in brain systems sub-serving these functions, such as thinner frontal and prefrontal cortex (Fortier et al., 2011; Mackey et al., 2018). In line with this, our research group has recently reported that dependent AAS users had thinner cortex in frontal and prefrontal regions, compared to non-dependent AAS users (Hauger et al., 2019b). However, the cognitive relevance and implications are largely unknown, and to our knowledge no study has tested for associations between EFs and AAS dependence. The present study assesses EF in dependent and non-dependent AAS users and non-using male weightlifters. We used a targeted battery of neuropsychological (NP) tests designed to assess different EFs, in addition to self-report questionnaires assessing EFs in everyday life. Moreover, we explored the relationship between self-report rating scales of EFs and NP test performance, ADHD symptoms and psychological distress. Based on previous research and models of EFs and dependency, we hypothesized that the AAS group would show poorer EF relative to non-using weightlifters, with stronger effects in dependent AAS users.

2. Materials and methods

2.1. Participants

Table 1 summarizes demographic and clinical characteristics of the sample. We included 174 adult male weightlifters who either had never used AAS or equivalent doping substances, or who reported previous or current AAS use corresponding to at least 1 year of cumulative AAS use (summarizing on-cycle periods). AAS users where further stratified based on AAS dependence criteria, yielding three groups: 1) AAS dependents; n = 58, 2) AAS non-dependents; n = 38 and 3) non-users; n = 78. The study sample is part of a longitudinal follow-up, where participants were asked to take part in a new investigation 3.5 years after first inclusion (52 % of the current sample) in addition to new participants being recruited (48 % of the current sample). The data included in the current paper was collected from April 2017 to September 2019. The participants were recruited through webpages and forums targeting people interested in heavy weight training, bodybuilding, and online forums directly addressing steroid use. Additionally, posters and flyers were distributed on selected gyms in Oslo. The study was approved by the Regional Committees for Medical and Health Research Ethics South East Norway (REC) (2013/601). All participants received an informational brochure with a complete description of the study prior to participation, and written informed consent was obtained from all participants. The participants were compensated for their participation with a gift certificate equivalent to 500 NOK (approximately 60$).

2.2. Interview and questionnaires

2.2.1. Demographics and substance use

Demographic and clinical data was assessed using a self-report questionnaire; where an excerpt is shown in Table 1. Current alcohol use was assessed with Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993), a 10 item self-report questionnaire. The generally accepted cut-point of for identifying a potential alcohol problem is 8 (Reinert and Allen, 2002), which provided us with the two following groups 1) “Alcohol risk-use” or 2) “Alcohol under-cutoff”.

Table 2
Test administered and which executive sub-function they tap.

Name of test / Test battery	Subtest	Function assessed	Component
Wechler Abbreviated Scale of Intelligence (WASI)	Block DesignMatrix Reasoning	Visuospatial reasoning Visual abstract problem-solving and reasoning	Problem-solving Problem-solving
Wechler Scale of Intelligence (WAIS)	Digit span	Auditory working memory	Working memory
Letter Memory Task (LMT)	LMT, computerized	Visual working memory	Working memory
Stroop Color-Word Interference test (CWIT), Delis-Kaplan Executive function system	CWIT 3 CWIT 4	Interference control Mental flexibility and interference control	Mental flexibility Mental flexibility
Trail Making Test (TMT), Delis-Kaplan Executive function system	TMT 4	Mental flexibility and shifting	Mental flexibility
The Stop Signal Task (SST), CANTAB, computerized	SSTSSRT	Response inhibition	Inhibition

The 11-item self-report Drug Use Disorders Identification Test (DUDIT) (Berman et al., 2005) was used to assess current non-AAS drug use, and the two following groups 1) "Drugs risk-use" or 2) "Drugs under-cutoff" was made based on a cutoff point of 6.

2.2.2. AAS use and dependence

The AAS users also completed digital self-report questionnaires mapping their AAS use, including motives behind their usage, age of onset, administration pattern, years of use, length of cycles and number of life-time cycles, side-effects, average weekly dosage, where in the cycle they were at the time of assessment, and whether and when they had ceased using AAS. The presence of AAS dependence was assessed by a structured clinical interview in the format of the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID II) by trained study personnel. The interview module is based on the substance-dependence criteria of DSM-IV, but modified to apply to AAS dependence (Kanayama et al., 2009). Adequate psychometric properties have been found (Pope Jr et al., 2010). The study participants were considered to be AAS dependent if they had a maladaptive pattern of AAS use causing clinically significant impairment or distress, manifested by three (or more) of the DSM-IV criteria (Kanayama et al., 2009).

2.2.3. Executive function in everyday life and ADHD symptoms

A short version of the self-report questionnaire Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A) (Roth et al., 2005) was used to asses executive functions in everyday life. Originally BRIEF-A consists of 75 items that comprise nine sub-scales that measure different aspects of executive functioning, measured on a three-point response scale; "never" (0), "sometimes" (1), and "often" (2). We selected the three questions with the highest correlation coefficient of each subscale; Inhibition, Shift, Emotional Control, Self-Monitor, Initiate, Working-Memory, Plan/Organize, Task-Monitor and Organization of Materials. Additionally we calculated a sum score by adding all the subscales. Since difficulties with EFs appear to be one important component of the complex neuropsychology of ADHD (Willcutt et al., 2005) and ADHD is associated with elevated risk for development of substance-use disorder (Biederman et al., 1995; Lee et al., 2011), we included the Adult ADHD Self-Report Scale (ASRS) v1.1. The ASRS is a symptom checklist developed by the World Health Organization (WHO) and is based on the ADHD diagnostic criteria of DSM-IV. The full version consists of 18 items, and the short screener is based on the six questions that were found to be the most predictive of symptoms consistent with ADHD (Kessler et al., 2005). Each item requires respondents to rate how frequently a particular symptom of ADHD occurred over the past six months on a five-point response scale from "never" (0) to "very often" (4). Based on the classification methods recommended by Kessler et al., (2005), (2007) a four-stratum classification were created: stratum I (score 0–9), stratum II (score 10–13), stratum III (score 14–17), and stratum IV (score 18–24). Also, a total sum score of all the eighteen items and a total inattention and hyperactivity-impulsivity score were obtained, as an equally weighted sum of response scores. The total ASRS score is shown to correlate significantly with clinician-rated overall symptom severity (Kessler et al., 2005).

2.2.4. Psychological distress

The Hopkins Symptom Checklist-25 (HSCL-25), derived from the 90-item Symptom Checklist (SCL-90) (Derogatis et al., 1974) was used to assess psychological distress. It consists of a 10-item subscale for anxiety and a 15-item subscale for depression, where each item is scored on a Likert scale from 0 (not at all) to 3 (extremely). A cut-off point (mean) of 1.75 indicates significant psychological distress and is widely used in research and practice (Glaesmer et al., 2014) although it has been argued that this cut-off point is too high for men (Sandanger et al., 1998).

2.3. Neuropsychological test assessment

The current paper used a selective battery of NP tests designed to assess different components of EFs. The following test was administered (see Table 2); Matrix Reasoning and Block Design from the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999), Digit Span WASI, Letter Memory Task (Morris and Jones, 1990), The Color-Word Interference test 3 & 4 (CWIT) and Trail Making tests 4 (TMT) from the Delis-Kaplan Executive function (D-KEFS) test battery (Delis et al., 2001),and The Stop Signal Task (SST) from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (De Luca et al., 2003; Goldberg, 2013). We classified the subtest into the four components, problem-solving, mental flexibility, working memory and inhibition. For the first three this was done by comprising the mean score of the z-transformed subtest included (see Table 2). For inhibition, the stop signal reaction time (SSTRT) represents the participant's mean stop signal delay at which he successfully inhibit his responses.

2.4. Statistical analysis

Comparisons of demographic data and self-reported executive function between the three groups were performed using One-Way ANOVA, and Chi square tests for categorical data. To compare characteristics related to AAS use between the AAS subgroups, two-tailed independent sample t-tests and Chi square test was used. We used Multivariate Analysis of Covariance (MANCOVA) to test for differences in neuropsychological test results, with test scores as dependent variable, group as independent variable, and age and education as covariates. Furthermore, to control for the possible influence of other substance use, we conducted analyses where risky alcohol and non-AAS drug use were included as covariates. Preliminary assumption testing was conducted, with no serious violations noted. Differences between the groups were considered to be significant at an alpha < 0.05. Partial eta-squared (ηp^2) and Cohen's d was used as an estimate of effect size. We corrected for multiple comparisons using Bonferroni correction for correlated measures (64) where the correlation between the dependent variables (the four executive components) is taken into account, ($\alpha_{original}$ 0.05 dived by 4 dependent variables with a Spearman's rho = .42 yielded $p_{adjusted} = 0.022$). The relations between various measures

of EF, ADHD scores and psychological distress were examined with Pearson's correlations. For scores on NP performance z-transformed residuals are used in the correlation analyses where variability associated with age and education is removed. All statistical analyses were conducted using SPSS version 25.0.0.1.

3. Results

3.1. Demographics and user characteristics

Demographic and other clinical data are presented in Table 1. The three groups did not differ in age or height. The AAS dependents had significantly lower IQ and fewer years of education, compared to both the non-dependents and the non-using weight-lifters. There was no significant between-group difference in risky alcohol use ($X^2 = 1.37$, $p = 0.505$), with the following distribution scoring over cut-off in each of the groups; 24.3 % of the non-users, 21.2 % of the AAS non-dependents and 15.7 % of the AAS dependents. However, there was a significant difference in risky non-AAS drug use ($X^2 = 21.32$, $p < .001$), with the highest percentage of risk use being in the AAS non-dependent group (29.0 %), compared to non-users (1.4 %) and AAS dependents (6.3 %).

Compared to AAS non-dependents, AAS dependents had significantly higher average weekly intake of AAS (mg/week), started using AAS at an earlier age and had a longer duration of use, see Table 1 for details.

3.2. Neuropsychological test assessment

Multivariate analysis of variance showed between-group differences on several EFs, independent of age and education, including working memory [F (2, 169) = 13.79, $p < .001$, $\eta p^2 = 0.14$], mental flexibility [F (2, 169) = 4.82, $p = .009$, $\eta p^2 = 0.05$], problem-solving [F (2, 169) = 4.77 $p = .010$, $\eta p^2 = 0.05$] and inhibition [F (2, 163) = 4.15, $p = .017$, $\eta p^2 = 0.05$]. After Bonferroni correction with an adjusted alpha value of 0.022, the effects remained with medium to large effect sizes, given by eta squared, for all the components. AAS dependents had the poorest performance on all measures, see Table 3 for details. AAS dependents performed significantly poorer compared to non-users, whereas AAS non-dependents did not differ significantly from non-users, except for working memory performance. The effects remained significant at an ordinal alpha level for working memory, mental flexibility and problem-solving after controlling for risky alcohol and non-AAS drug use, see Table 5.

3.3. Self-report questionnaires

3.3.1. Executive function in everyday life

There were significant between-group differences on self-reported problems with executive functions in everyday life, for the total BRIEF score [F (2, 135) = 6.89 $p = .001$, $\eta p^2 = 0.09$] and the following subscales; Inhibition, Shift, Emotional Control, Self-Monitoring, Initiation, Working Memory and Organization of Materials. Bonferroni post hoc test show that AAS dependents reported significantly more problems compared to non-users, whereas AAS non-dependents did not differ significantly from non-users, except for inhibition and working memory, see Table 4 for details. Significant between-group differences remained on the total BRIEF score after controlling for risky alcohol and non-AAS drug use, see Table 5.

3.3.2. ADHD symptoms

There was significant between-group differences on self-reported ADHD symptoms, measured by the total ARSR score [F (2, 135) = 8.58 $p = .001$, $\eta p^2 = 0.11$], the inattention subscale [F (2, 135) = 5.78 $p = .004$, $\eta p^2 = 0.08$], and the hyperactivity-impulsivity subscale [F (2, 135) = 9.89 $p < .001$, $\eta p^2 = 0.13$]. AAS dependents scored significantly higher compared to the non-users, whereas AAS non-dependents did not differ significantly from non-users. Significant between-group differences remained on the total ARSR score after controlling for risky alcohol and non-AAS drug use, see Table 5. There was no significant difference in ASRS strata classification between the groups ($X^2 = 5.53$, $p = .478$). The majority of all the groups were in Strata I and II, the following percentages were in Strata III, non-users (1.5 %), AAS non-dependents (6.9 %) and AAS dependents (6.8 %) and in Strata IV; non-users (1.5 %), AAS non-dependents (3.4 %) and AAS dependents (4.5 %).

3.3.3. Psychological distress

There were significant between-group differences on self-reported problems with psychological distress, for the total HSCL score [F (2, 135) = 4.73 $p = .010$, $\eta p^2 = 0.07$], the anxiety subscale [F (2, 135) = 5.57 $p = .005$, $\eta p^2 = 0.08$] and the depression subscale [F (2, 135) = 3.38 $p = .037$, $\eta p^2 = 0.05$]. AAS dependents reported significantly more symptoms compared to non-users. Significant between-group differences remained on the total HSCL score after controlling for risky alcohol and non-AAS drug use, see Table 5. Additionally, a higher percentage of the AAS dependence (22.7 %) scored over clinical cut-off (≥ 1.75), compared to non-users (4.6 %) and AAS non-dependents (13.8 %), ($X^2 = 8.04$, $p = 0.018$).

3.3.4. Correlations between self-report and NP tests

There were strong significant correlations between self-reported problems with EFs and total ADHD symptoms, ($r = .767$, $p < .001$), and psychiatric symptoms ($r = .769$, $p < .001$). There was no significant correlation between NP test results and the self-report measures, see Fig. 1 for details.

4. Discussion

The present study examined EFs in a large sample of AAS-exposed and non-exposed weightlifters. The AAS dependents exhibit poorer EFs in both test setting and every-day life, compared to non-using weightlifters. Self-reported executive dysfunction was associated with ADHD symptoms and psychological distress. Potential implications are discussed below.

Table 3
Executive function test results.

		Non-user ($n = 78$)	Non-dependent ($n = 38$)	Dependent ($n = 58$)	Main effect of group		
	α	Mean z (*SD*)	Mean z (*SD*)	Mean z (*SD*)	F	*p-value*	ηp^2
Problem-solving	.72	.328 (72)	.016 (88)	−417 (91)	4.77	.010[a]	.05
Working memory	.77	.437 (.78)	−.033 (78)	−.522 (84)	13.79	< .001[ac]	.14
Mental flexibility	.75	−.272 (.68)	.110 (.94)	.280 (.78)	4.82	.009[a]	.05
Inhibition		208.8 (30.4)	208.0 (36.8)	228.4 (35.5)	4.15	.017[ab]	.05

α = Cronbach's alpha. Problem-solving and working memory, higher score reflects better performance. Mental flexibility and inhibition, higher score reflects poorer performance. Bonferroni post hoc test; a = AAS dependents significantly different from non-users, b = AAS dependents significantly different from AAS non-dependents and c = AAS non-dependents significantly different from non-users.

Table 4
Executive function self-report.

		Non-user (n = 65)	Non-dependent (n = 29)	Dependent (n = 44)	Main effect of group		
	α	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	*F*	*p-value*	ηp^2
BRIEF Total	.93	8.09 (7.71)	12.86 (9.89)	14.52 (10.94)	6.89	.001[a]	.09
Inhibit	.60	0.97 (1.05)	1.83 (1.34)	1.84 (1.54)	7.85	.001[ac]	.10
Shift	.63	0.75 (1.13)	0.97 (1.15)	1.55 (1.41)	5.53	.005[a]	.08
Emotional control	.71	0.86 (1.14)	1.21 (1.08)	1.77 (1.64)	6.34	.002[a]	.09
Self-Monitor	.64	0.71 (0.91)	1.07 (1.10)	1.34 (1.40)	4.25	.016[a]	.06
Initiate	.80	1.48 (1.47)	2.03 (1.86)	1.73 (1.83)	1.14	.323	.02
Working Memory	.74	0.82 (1.09)	1.69 (1.79)	2.07 (1.87)	9.44	< .001[ac]	.12
Plan/organize	.78	0.68 (1.15)	1.21 (1.42)	1.09 (1.36)	2.30	.104	.03
Task Monitor	.77	1.02 (1.23)	1.66 (1.49)	1.64 (1.63)	3.35	.038	.05
Organization Materials	.74	0.82 (1.06)	1.21 (1.52)	1.50 (1.59)	3.46	.034[a]	.05
HSCL Total	.92	1.23 (.30)	1.37 (.39)	1.44 (.45)	4.73	.010[a]	.07
HSCL Anxiety	.85	1.16 (.27)	1.32 (.36)	1.40 (52)	5.57	.005[a]	.08
HSCL Depression	.88	1.27 (.35)	1.40 (.43)	1.47 (45)	3.38	.037[a]	.05
ADHD Total	.90	16.7 (8.3)	21.1 (11.7)	25.4 (13.2)	8.58	< .001[a]	.11
ADHD Inattention	.84	8.9 (5.0)	11.3 (6.4)	12.8 (7.3)	5.78	.004[a]	.08
ADHD Hyper-impulsive	.81	7.8 (4.3)	9.8 (5.6)	12.5 (6.6)	9.89	< .001[a]	.13

α = Cronbach's alpha. Bonferroni post hoc test; a = AAS dependents significantly different from non-users and c = AAS non-dependents significantly different from non-users.

Table 5
Main findings adjusted for alcohol and non-AAS drug use.

	Main effect of group		
	F	*p-value*	ηp^2
Mental flexibility	3.35	.038[a]	.05
Working memory	10.78	< .001[a]	.13
Problem-solving	3.83	.024[a]	.05
Inhibition	2.82	.096	.03
BRIEF total	9.26	< .001[ab]	.12
HSCL total	6.03	.003[ab]	.09
ADHD total	12.7	< .001[ab]	.17

Bonferroni post hoc test: a = AAS dependents significantly different from non-users and b = AAS dependents significantly different from AAS non-dependents.

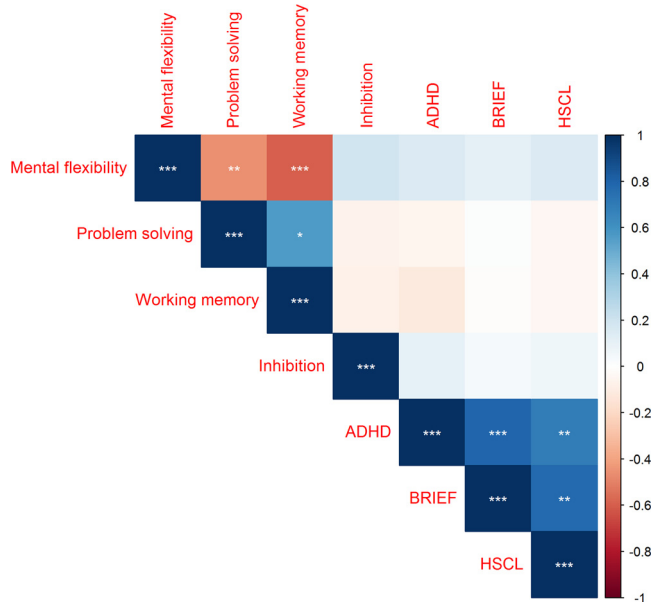

Fig. 1. Correlation between performance-based executive functioning and self-report measures of executive function, psychological distress and ADHD symptoms. ADHD, BRIEF and HSCL each represent the total scale score. *p < .05, **p < .01, ***p < .001.

4.1. AAS dependents significantly different, as opposed to non-dependents

In accordance with previous studies (Hauger et al., 2019a; Kanayama et al., 2009c), AAS-users fulfilling the criteria for AAS-dependency were, on a group level, clearly different from non-dependent AAS users and non-exposed weightlifters on several measures. On NP measures AAS dependents performed markedly poorer on inhibition, working memory, mental flexibility and problem-solving tasks, compared to non-using weightlifters. The dependent group also reported significantly more problems with working memory, initiation, mental flexibility, inhibition, self-monitoring and emotional control in everyday life. The non-dependent group did not differ to the same extent. On most measures the non-dependents were not significantly different from non-using weightlifters. The exceptions included higher scores on the BRIEF-A working memory and inhibit scale, indicating more difficulties with controlling impulses, and lower working memory performance compared to non-exposed weightlifters. These findings are in line with previous reports of other drug dependencies stating that executive deficits in individuals with a dependency syndrome typically is more generalized and of greater magnitude, compared to what have been seen for recreational users (Verdejo-García and Pérez-García, 2007). Furthermore, the AAS dependents had lower IQ, which might be related to the observed effects. The majority of participants across groups reported relatively few ADHD symptoms (strata I and II), which indicates a low probability for the presence of an ADHD diagnosis. Still, the dependent group reported significantly more ADHD symptoms compared to the non-users. There is evidence suggesting that ADHD comprises a dimensional trait, where an increase in number of symptoms is associated with higher comorbidity and disability (Vogel et al., 2018). Furthermore, even few ADHD symptoms are associated with an increased burden, and differences seen at a subclinical level might be clinically relevant. Consistent with this there was a significant strong positive correlation between ADHD symptoms and self-reported problems with EFs and psychological distress, emphasizing the important link between self-reported EFs and psychological wellbeing.

4.2. Executive functions, behavior and psychological distress

EF skills are essential for mental and physical health and adaptive social functioning. AAS dependence has been associated with intra- and interpersonal problems (Hauger et al., 2019a; Kanayama et al., 2009c)

and high levels of involvement in aggressive and antisocial behaviors (Copeland et al., 2000; Kanayama et al., 2009c), that might be partly related to executive dysfunction such as reduced inhibitory control, self-monitoring and emotional regulation. Also, dysfunctional executive control may increase the likelihood of drug-seeking behavior despite repeatedly adverse outcomes on psychical, emotional and social well-being. For instance may difficulties with problem-solving and decision-making increase the likelihood of guiding behavior based on available short-term gains, rather than on careful consideration of the long-term consequences of their choices (Passetti et al., 2008). This cognitive style may negatively affect both the individual and their social relations.

In the present study the AAS dependents experienced more psychological distress. The AAS dependents reported higher levels of both anxiety and depression, and over 20 percent scored above clinical cut-off indicating significant distress. These results are consistent with previous results from our research group and others demonstrating that AAS dependence is associated with heightened levels of mental health problems (Brower, 2009; Hauger et al., 2019b; Kanayama et al., 2009c). There are evidence suggesting a dose-response relationship between AAS use and psychological effects, in the sense that psychological effects are related to the type, combinations, doses and duration of use (Kanayama et al., 2008; Pagonis et al., 2006). The AAS dependents had a higher cumulative AAS lifetime exposure, which may be linked to an increased risk of adverse psychological effects. Furthermore, it has been argued that the motivation for persistent use despite adverse consequences is sustained in large parts by psychological factors, highlighting the importance of healthcare professional having an understanding of these psychological variables, including the potential for AAS to cause dependence (Brower, 2009). Indeed, mental health problems seem to be the main reason for AAS users to seek treatment and should receive considerable attention (Havnes et al., 2019)

4.3. Executive dysfunction and vulnerability for use and dependence

Several neuroimaging studies demonstrate that substance abuse is associated with brain abnormalities in frontal and prefrontal regions (Bolla et al., 2004; Fortier et al., 2011; Mackey et al., 2018). These regions are typically assumed to reflect important nodes in the extended brain network supporting executive functions (Miller and Cohen, 2001). In line with this, our research group recently reported that dependent AAS users had thinner cortex in widespread regions, specifically in frontal and prefrontal regions, compared to non-dependent AAS users (Hauger et al., 2019b). Thus, assuming a link between brain structural variability and cognitive performance, it was anticipated that the dependent group exhibited problems with EF to a greater extent. The dependent group had used AAS for a longer period, and had a higher cumulative AAS lifetime exposure, that might be related to the observed effects. However, the cross-sectional design does not allow claims regarding causality. Thus, we cannot infer whether the observed effects are due to pre-existing factors or long-term AAS use. Presumably, pre-existing cognitive, genetic and environmental factors predict initial AAS use, and the development of a dependency syndrome might reflect a combination of pre-existing vulnerability and consequences of escalated use. It has previously been reported that conduct disorder represents an important risk factor for initiating AAS use among male weightlifters (Pope Jr et al., 2012) as well the progression to AAS-dependence (Kanayama et al., 2018). Here, we see that also ADHD symptoms at a subclinical level is associated with AAS-use and dependence, and although not possible to determine with cross-sectional data, might pose an early risk for AAS initiation and progression of use.

4.4. Considering executive functions in the context of treatment and rehabilitation

It is critical to consider executive dysfunction in relation to treatment and rehabilitation, since EF is associated with treatment retention and drug relapse (Aharonovich et al., 2006; Brorson et al., 2013; Passetti et al., 2008). Adequate cognitive functioning is essential for many of the activities in psychosocial therapies commonly used in SUD treatment (Aharonovich et al., 2006; Gottschalk et al., 2001). Consequently, neuropsychological assessment could give useful information to guide treatment planning. Together with other clinical measures, neuropsychological test results may be used to identify individuals in need of specifically adjusted treatment programs and or cognitive rehabilitation (Brorson et al., 2013; Passetti et al., 2008). Furthermore, clinically it is important to consider which methods to use when assessing EF on an individual level. Our results showed no significant correlations between the NP EF tests and self-reported EF (BRIEF-A), suggesting that they capture different aspects of functioning. This coincides with previous studies reporting that BRIEF-A is associated with emotional distress, but not performance-based EF tests (Hagen et al., 2019; Løvstad et al., 2016). Together this emphasizes the importance of taking both test results and self-report into account when conducting an evaluation of overall functioning. Many AAS users describe a reluctance to seek treatment, partly because they perceive health-care professionals to lack knowledge about AAS use and its consequences (Pope et al., 2004). Furthermore, although AAS-dependence share features with other substance dependencies, there are also marked differences (Hildebrandt et al., 2011), meaning that treatment programs need to be adjusted to apply to AAS dependence. Thus, improved knowledge about specific features of AAS dependence needs to be implicated in clinical practice. Moreover, it is important to note that although we find significant differences between the groups on several accounts, there is always variation within the groups. The variation and the individual perspective are important to recognize, especially in clinical practice. It is crucial to be curious and explore the motives behind the AAS use, and as with every other drug of abuse, explore the function the AAS use has for the individual.

4.5. Limitations

There are some limitations to the present study. First, the study sample had a high proportion of AAS dependents compared to other studies. However, many of the participants were long-term users, and dependent users reported using AAS for 13.3 years on average. Thus, the high proportion of dependents may be seen in relation to the increased likelihood of developing dependence upon prolonged use. Second, the cross-sectional design does not allow claims regarding causality. Third, while the Cronbach's alpha for the total scale scores is indicative of excellent internal consistency, there is some variability for the subscales, ranging from questionable to good, questioning the generalizability of the subscale findings. Fourth, drug dependencies are complex phenomena with a highly multidimensional origin. Even if we statistically control for relevant confounders, confounding may still exist, e.g. through clinical features not assessed as part of this project or through interactions between clinical variables.

4.6. Conclusion

AAS dependence is associated with executive dysfunction in both test setting and every-day life as assessed using self-reports. The latter was strongly associated with ADHD symptoms and psychological distress. AAS dependents seem to be a vulnerable population, where problems with EF might be one of many factors related to the development and maintenance of dependence. Increased awareness of executive dysfunction could have important implications for treatment and rehabilitation.

Author disclosures

The presented results have not been previously published, and no

related papers are under submission or revision in any other journals. All authors have contributed substantially to the present work and have seen and approved the manuscript being submitted. All authors declare no conflict of interest.

Contributors

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Declarations of Competing Interest

None.

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Appendix A. Supplementary data

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