Author's response to reviews

Title: Life Context of Pharmacological Academic Performance Enhancement among University Students - a Qualitative Approach

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Author's response to reviews: see over
Dear Madam, dear Sir,

Please find attached the revised version of the manuscript „Life Context of Pharmacological Academic Performance Enhancement among University Students – a Qualitative Approach“.

Below you find our comments to reviewers’ reports.
We modified the manuscript according to the reviewers' suggestions and hope that you now find it suitable for publication.

Yours sincerely

(PD Dr. Elisabeth Hildt)
Comments to Reviewers’ reports:

Hildt et al.:
Life Context of Pharmacological Academic Performance Enhancement among University Students - a Qualitative Approach.

Reviewer: Jayne Lucke

This paper examines the experiences of 18 healthy university students reporting the non-medical use of prescription and illicit stimulants for academic performance. The stated aim of examining this type of “cognitive enhancement” in a broader context is of value. Furthermore, the evidence-base required to inform policy and practice in this area is weak so empirical research is welcomed. Unfortunately the data analysis and presentation of the paper fails to meet the worthy goal and consequently doesn’t advance the field adequately to justify publication.

1. The authors have published in this field (and specifically, from this data) before and consequently will be familiar with the debates surrounding cognitive enhancement in the bioethics literature. Unfortunately this depth of knowledge is not reflected in the background of the paper. To warrant publication the background section should clearly articulate the state of the field, which particular gaps the paper addresses, and how it will advance the field.

➔ We reworked the background section (cf. pages 4-6), added relevant information on the state of the field, in particular on the aspects we are interested in, explicitly described the gaps the paper addresses and how the paper will advance the field.

Related to this issue:

a. The background provides a broad description of various issues relating to the debate around cognitive enhancement such as: limited scientific evidence to support improvements in cognitive ability, concerns about safety and side effects, range of definitions, prevalence estimates. However, the focus should be more specifically on what is known about motivations for non-medical use of stimulant. The background should build a stronger case for examining such use within a broader context. Too much ground is covered in a superficial manner without adequately justifying the rationale for the study that was conducted.

➔ We met this point by extensively modifying the background section of the paper.
b. Another example can be found half way down page 5 where the case is put that such stimulant use for academic purposes might not be expected to be prevalent given the limited pro-cognitive effects, sizeable side effects and illegality. The assumption that students would be fully aware of these issues, when many others are not is naive (e.g. the first sentence of the paper notes the considerable media attention generated over the past few years). Much media attention has been overly positive, and could lead to the impression that “smart drugs” are effective.

→ On page 5, we modified the paragraph in question as follows:
“The prevalent use of potential cognitive enhancing drugs on high school and university campuses seems surprising in light of the very limited pro-cognitive effects and sizeable side effects described in literature and given the illegality of misusing prescription and illicit drugs. Several reasons can be assumed for the current interest in so-called pharmacological cognition enhancers in academic contexts [11]. One reason may be recent media hype on the putative cognition-enhancing effects of psychostimulants which may have resulted in the assumption among students that psychostimulants serve to increase academic performance [1, 25]. Another reason may be that there is a benefit for at least part of the users, but that up to now this benefit is not adequately reflected in literature. It is also possible that for genetic or other reasons, part of the healthy population is particularly susceptible to cognition-enhancing effects of psychostimulants. Alternatively, there may be a non-cognitive effect of psychostimulant intake that students consider of value in academic contexts [11, 12].”

2. The distinction between prescription and illicit stimulants is an important one that needs more attention in the background. There are important differences in the legal consequences, methods of acquisition, costs, and health risks that should be acknowledged.

→ Regarding this valuable advice, we inserted the aspect of the difference between the use of prescription and illicit stimulants in the introduction section as follows:
“Beyond that, the distinctions between the use of prescription stimulants and illicit stimulants concerning safety risks, methods of acquisition, legal consequences and costs have to be regarded. In this respect the legal and health risks of the use of illicit stimulants seem to be much higher than of the use of prescription stimulants.”

3. The referencing need to be done more carefully. Use carefully chosen references for specific points, rather than multiple references for general statements.
According to the reviewer’s comment we carefully checked the referencing throughout the manuscript and adapted the references in the whole manuscript.

4. The analysis is descriptive, and consequently does not get to the heart of the question of why students use stimulants and how their use in academic environments can be viewed in the broader context. For example, in the results Category 1 examines context – it appears that there is a common theme in this category: that students are using the stimulants to “get things done”. What those things are depends on what the student wants to do, whether that is getting through academic work, composing music, playing computer games, etc. The underlying motivation would appear to be the same. The other motivation appears to be “feeling good/having fun” which overlaps with the motivation to “get things done” when the students want to “feel good while getting things done”. More nuanced exploration of these motivations would add to the value of the paper and enhance the goal of exploring the context of student use of stimulants.

We followed this helpful suggestion and added the following sentences which sum up our results concerning the users’ motivations:

“Taken together, among the main motivations for non-medical use of stimulants by students seem to be the motivation to get things done, be it in order to meet academic demands or to have a fulfilling leisure time, and the motivation to feel active and energetic while performing their tasks. This supports the findings by Partridge and colleagues [28].”

5. Another aspect of the analysis that could be further developed is the way that students appear to be using stimulants when they haven’t prepared for exams or done adequate work in time. An interesting ethical question is whether the use of stimulants could be seen as a way of bringing disorganized or unmotivated students up to a level of achievement that is similar to well-organized motivated students. What is the evidence for this, and what are the implications? A related question is to what extent students are self-medicating for symptoms of depression? Is stimulant use for study a marker for poor mental health?

These are very interesting questions, indeed. However, our data does not allow us to reflect on these in more detail. This will be research questions for future studies.

6. One participant developed addictive behaviour (p13). It would be interesting to know more about the context of this. Given the qualitative nature of the study a more detailed exploration of the circumstances of this addiction could open fruitful avenues of enquiry in further studies.
On page 20 we refer to work in progress in which aspects relating to addiction and to the users’ views on the risk of addiction will be discussed in detail.

7. The study is based on a small sample of 18 students. While the smallness of the sample is not a problem in itself for qualitative research, the potential limits to generalizability should be discussed more specifically, i.e. what types of students may have been missed because of the direct recruitment of students who have used stimulants for study. The recruitment strategy may have resulted in a bias towards students who viewed their use in a particular way (i.e. they were happy to be identified as users, and happy to discuss their use in a research study). The implications for the interpretation of the findings should also be discussed.

On page 20/21, we added the following two paragraphs in order to discuss potential limits to generalizability more specifically:

“The “type” of student willing to participate may display the main bias of the small group of participants. Participants had to be frequently enough at the campus, had to have enough time for the interview study, had to be interested in participating in scientific studies, had to be convinced about the importance of the CE phenomenon, had to take the risk to talk about their illegal behavior without being punished, etc. This kind of a “self-selection” of participants may have led to a certain bias in the composition of the group of participants.

In addition, the exclusion of students with psychiatric disorders and current physicians’ prescriptions of psychoactive medication leads to bias implying that the present study is not representative for the entirety of students. The prevalence rate of psychiatric disorders among the population is high – e.g. 5.3% for ADHD among children/adolescents, 4.4% among adults [34, 35]. All these students have been excluded which displays an important bias. However, it was not the aim of this study to explore CE aspects among patients but among healthy subjects. Including ADHD patients would have meant to include participants with a totally different context of stimulant use (misuse of own prescription medication) and would have diluted the distinction between therapy of disorders and enhancement of healthy people’s abilities. It is questionable whether we excluded potential participants who faked or exaggerated ADHD symptoms for a prescription of stimulants by a physician.”

8. One specific source of bias that should be directly addressed is the exclusion of students with a current physicians’ prescription of psychoactive medication. This excludes students who might have obtained a prescription for the purposes of academic work by faking or exaggerating symptoms of a disorder. The literature suggests that this may be one way that students at-
tempt to gain a legitimate prescription (albeit for an illegitimate use), or alternatively may be related to experiencing milder symptoms of a legitimate disorder such as ADHD. In-depth examination of these complex, overlapping issues is outside the scope of the paper, but the implications for the nature of the sample and the interpretation of the results should be discussed.

→ We discussed this aspect as follows, cf. point 7:

“In addition, the exclusion of students with psychiatric disorders and current physicians’ prescriptions of psychoactive medication leads to bias implying that the present study is not representative for the entirety of students. The prevalence rate of psychiatric disorders among the population is high – e.g. 5.3% for ADHD among children/adolescents, 4.4% among adults [34, 35]. All these students have been excluded which displays an important bias. However, it was not the aim of this study to explore CE aspects among patients but among healthy subjects. Including ADHD patients would have meant to include participants with a totally different context of stimulant use (misuse of own prescription medication) and would have diluted the distinction between therapy of disorders and enhancement of healthy people’s abilities. It is questionable whether we excluded potential participants who faked or exaggerated ADHD symptoms for a prescription of stimulants by a physician.”

9. Overall there needs to be a much stronger case presented regarding: What does this paper contribute that is not already known? How do the findings add to knowledge, and advance the field?

→ Cf. our answers to the reviewer’s points 1-8 and the extensive modification of the background section. In addition, the following sentences were written to compare the results obtained with the current state of knowledge:

p. 18: “[Strikingly, both studies indicate that, for the users, the main motive for stimulant use is to be able to handle the demands of university, in particular, with regard to the practical, motivational and emotional aspects of studying and preparing for exams.] This is in perfect line with a recent study by Ilieva and Farah (2013) who found out that students who used psychostimulants for enhancement perceived motivational advantages of stimulant use to be at least as pronounced as cognitive effects [11].”

p. 19: “[This concurs with the idea that psychostimulant use is associated with the overestimation of one’s own capabilities.] The results obtained here are in accordance with a recent quantitative study on the effects of mixed amphetamine salts on healthy young adults [8]. Overall, the study did not reveal significant enhancement effects on cognitive performance in a set of 13 measures of cognitive ability examined. Nevertheless, compared to those who received a
placebo pill, those who had taken a stimulant pill believed their cognitive performance to be
more enhanced.

It is important to keep the distinction between objective effects and subjective perception of
effects in mind as it may help us to avoid an over-optimistic picture of the purported positive,
cognition-enhancing effects of stimulants."

10. What are the implications for future research? What do we need to know and how should
we go about finding out? For example, why do students NOT use drugs to enhance their pe-
formance, and what strategies do good students use instead? This could be an important ques-
tion to be addressed by future research about the broader context of student drug use.

→ Concerning the implications for future research, in the conclusions section on page 22 we
added the following:
“[More research needs to be carried out to better understand the practice and context of aca-
demic performance enhancement. The results obtained here may serve as a starting point for
future qualitative and quantitative research.] It will be necessary to know more about the stu-
dents’ motivations for pharmacological neuroenhancement and about its objective effects on
academic performance achieved. In addition, research should be done on drug use put in the
context of other strategies for coping with pressure to perform in academic contexts which will
include questions such as: What other ways are there to cope with pressure that do not involve
the misuse of drugs? To what extent does society play a role in the field of neuroenhancement?
All of this will form the basis for future policy recommendations concerning pharmacological
neuroenhancement."

Reviewer: Peter Bart Reiner

I know that it is ‘allowed’, but I found the repeated quantitative citation of the number of observ-
ations of each remark in a paper using qualitative methods to detract from the richness of the
results. Reporting that 4 individuals said “X” while 7 individuals said “Y” is not really mean-
ingful, and certainly the authors do not make claims that remark “Y” made by the 7 are more
relevant than remark “X” made by the 4. Indeed, the authors are clear in their disclaimer at the
end of that the results cannot be generalized. I know that adding numerical precision in qualita-
tive results is allowed, but I think it should only be used when it adds to the veracity of the results; in this case it does not. I would be happy to hear arguments that suggest otherwise, but unless the authors can provide them, I suggest they remove the quantitative and allow this qualitative study to rest on its own merits.

→ The authors removed quantitative data from the results and discussions section (except the first sections of the results containing participants’ characteristics).

**Reviewer: Three**

This qualitative study of University students’ perspectives on the use of pharmacological cognitive enhancers (PCEs) is based upon the same data set as two previous ‘preliminary studies’ by the same authors (Franke AG, Lieb K, Hildt E: What users think about the differences between caffeine and illicit/prescription stimulants for cognitive enhancement. PLoS One 2012, 7:e40047; Hildt E, Franke AG, Lieb K: Pharmacological neuroenhancement: Information and acceptance among students. Nervenheilkunde 2011, 10:833-837.) The results are clearly distinct from those reported in the previous two manuscripts.

The authors used inductive category development to identify 6 ‘categories’ of comments that are considered to represent the impact of using PCEs on the students personal lives – both within the context of university studies and that of their lives as a whole. Using this approach, they present qualitative results of their interviews with extensive quotation from the students themselves. The major observation is congruent with those of other recent studies: students do not perceive that PCEs provide a major benefit with respect to cognitive function, but that they do provide a benefit with regard to motivation to complete the task. The authors are fastidious about citing other qualitative work with similar results; they may wish to consider recent quantitative work which arrives at similar conclusions (Ilieva I, Boland J, Farah MJ. Objective and subjective cognitive enhancing effects of mixed amphetamine salts in healthy people. Neuropsychopharmacology. 2013 Jan;64:496–505. Ilieva IP, Farah MJ. Enhancement stimulants: perceived motivational and cognitive advantages. Front Neurosci. 2013;7:198.) Given the congruence of findings emerging from different research groups, this seems to be a robust, reproducible, and likely important observation. For this reason alone, this manuscript deserves to be published. Overall, the writing is clear, the data is sound, and the study a valuable contribution to the literature.
Thank you very much for this very valuable comment!

In the background section, we discussed the findings by Ilieva et al. 2013 and by Ilieva and Farah 2013. In particular, we added:

p. 4: “A recent study revealed the lack of enhancing effects of mixed amphetamine salts on cognitive abilities in healthy young individuals [8]. In spite of this, in anecdotal reports and quantitative and qualitative studies users said to subjectively experience positive effects on cognition [8-10]. In addition, growing evidence indicates that healthy users perceive motivational and emotional effects to be of value in the non-medical use of psychostimulants [11, 12].”

p. 5/6: “The prevalent use of potential cognitive enhancing drugs on high school and university campuses seems surprising in light of the very limited pro-cognitive effects and sizeable side effects described in literature and given the illegality of misusing prescription and illicit drugs. Several reasons can be assumed for the current interest in so-called pharmacological cognition enhancers in academic contexts [11]. One reason may be recent media hype on the putative cognition-enhancing effects of psychostimulants which may have resulted in the assumption among students that psychostimulants serve to increase academic performance [1, 25]. Another reason may be that there is a benefit for at least part of the users, but that up to now this benefit is not adequately reflected in literature. It is also possible that for genetic or other reasons, part of the healthy population is particularly susceptible to cognition-enhancing effects of psychostimulants. Alternatively, there may be a non-cognitive effect of psychostimulant intake that students consider of value in academic contexts [11, 12].”

p. 6: “A recent quantitative study by Ilieva and Farah provides support to the hypothesis that there may be non-cognitive effects of psychostimulant intake that are considered as advantages by healthy individuals [11].”

In the discussion section, we compared our results with the results by Ilieva et al. 2013 and Ilieva and Farah 2013 as follows:

p. 18: “This is in perfect line with a recent study by Ilieva and Farah (2013) who found out that students who used psychostimulants for enhancement perceived motivational advantages of stimulant use to be at least as pronounced as cognitive effects [11].”

p. 19: “The results obtained here are in accordance with a recent quantitative study on the effects of mixed amphetamine salts on healthy young adults [8]. Overall, the study did not reveal significant enhancement effects on cognitive performance in a set of 13 measures of cognitive ability examined. Nevertheless, compared to those who received a placebo pill, those who had taken a stimulant pill believed their cognitive performance to be more enhanced.
It is important to keep the distinction between objective effects and subjective perception of effects in mind as it may help us to avoid an over-optimistic picture of the purported positive, cognition-enhancing effects of stimulants.”