Teacher Standardisation

Spring 2018

L3 Extended Project Qualification (7993)

Project 4

AQA
Realising potential

2016/17 candidate record form, production log and assessment record

Level 3 Extended Project (7993)

Please attach the form to your candidate's work and keep it at the centre or send it to the moderator as required. The declarations should be completed as indicated.

Centre number	**Centre name**

Candidate number	**Candidate's full name**

Work submitted for assessment **must** be the candidate's own. If candidates copy work, allow candidates to copy from them, or cheat in any other way, they may be disqualified.

Candidate declaration

Have you received help/information from anyone **other than** subject teacher(s) to produce this work?

☐ No ☐ Yes *(give details below or on a separate sheet if necessary).*

I contacted a specialist in the field to have an in depth conversation about the topic at hand to give me greater understanding of the subject matter.

Please list below any books, leaflets or other materials (for example DVDs, software packages, internet information) used to complete this work **not** acknowledged in the work itself. Presenting materials copied from other sources **without acknowledgement** is regarded as deliberate deception.

Click here to enter text.

From time to time we use anonymous examples of candidates' work (in paper form and electronically) within our guidance materials to illustrate particular points. If your work appears in AQA materials in this context and you object to this, please contact us and we will remove it on reasonable notice.

I have read and understood the above. I confirm I produced the attached work without assistance other than that which is acceptable under the scheme of assessment.

te signature. Date Click here to enter a date. 3/5/17

Supervisor declaration

I confirm the candidate's work was conducted under the conditions laid out by the specification. I have authenticated the candidate's work and am satisfied, (to the best of my knowledge) that the work produced is solely that of the candidate.

ignature. Date Click here to enter a date. 3/5/17

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Submission checklist

To be completed by the supervisor

Extended Project **working** title: Click here to enter text. To what extent do genetic factors contribute to a propensity towards addiction?

Extended Project **final** title: Click here to enter text. To what extent do genetic factors contribute to a propensity towards addiction in humans?

Form of project

☑ Either written report

☐ Or Click here to enter text. and accompanying written report

Is this project part of a group project?

☑ No

☐ Yes If 'Yes', give brief details Click here to enter text.

Please note that failure to complete or submit a compulsory element may result in a mark of zero being awarded.

Select/tick	Items that **must** be included	Notes
☑	1. A signed and completed *Candidate record form, production log and assessment record*	This document. All pages must be completed.
☑	2. Research based written report	If the project product is an artefact or a production, an accompanying research based written report is also required.
☑	3. Evidence of the project product	Eg photographs of artefact, investigation or production; a piece of creative writing (artefact); research based written report.
☑	4. Evidence of a presentation within the production log	Presentation on the project process. Where the project product is itself a presentation (for a specified audience), a presentation on the project process must also be delivered to a non-specialist audience

EPQ 2016-17 Taught Elements

Date	Content
14/6/16	EPQ launched in assembly with Year 12 students following their return from exam leave
22/6/16	Afternoon session with all interested students to cover process of completing an EPQ in more detail
w/c 4/7/16	All students seen for brief discussion of their topic idea prior to undertaking research over the summer term.
5/7/16	School librarian completes a session on effective research skills with all students on EPQ.
12/10/16	All students visited Sheffield University for a day. 2 hours spent looking at research skills and methodology. 4 hours spent in the University library accessing the university book stack and catalogue.
28/11/16	What makes a good project-guidance on writing up research and how this should be structured.
23/1/17	What makes a good presentation-input around presentations and how these should be structured.
30/1/17	How do I reference my research? Session on Harvard referencing

In addition to the above, all students had weekly sessions timetabled with their supervisors. Most groups were split into two and seen on an individual basis on a fortnightly timetable to allow discussion of individual project progress.

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

The taught skills element

To be completed by the supervisor

Outline details of taught skills

Record here details of relevant skills taught in a class/group and details of relevant skills taught individually to this candidate as described in the specification. Continue on a separate sheet if necessary.

Click here to enter text.

Candidate number Click here to ente

Candidate's full name Click here to enter text.

Record of marks

To be completed by the supervisor
Marks must be awarded in accordance with the instructions and criteria in the specification.

Summary information to show how the marks have been awarded should be given in the spaces below in addition to comments in other pages of this document and any supporting information in the form of annotations on the candidate's work.

Skill area	Maximum mark	Mark awarded	Supervisor's supporting statement
A01 Manage	10		
A02 Use resources	10		
A03 Develop and realise	20		
A04 Review	10		
Total mark	50		

Supervisor's concluding comments
Click here to enter text.

Internal moderation comments if appropriate
Click here to enter text.

Supervisor declaration
I confirm that no work assessed for the award of the marks above is also to be submitted, or has been submitted, for any other accredited qualification(s).

Supervisor signatur

Date Click here to enter a date. 3/5/17

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Record of initial ideas

To be completed by the candidate
This page records initial meeting(s) with your supervisor to agree your project ideas. Additional pages can be submitted if more than one idea has been explored.

My idea(s) for topic/title

Due to my fascination with the disorder of addiction, and my strong grounding in scientific knowledge, I have decided to base my project on some facet of addiction. I am currently considering exploring the nature nurture debate of addiction in a comparative study.

An initial idea for my project is: Is susceptibility to alcohol (or nicotine) based in genetics or environmental factors.

My ideas for research and development of my project

- Investigating environmental factors such as aspects of family life: divorce, aggression in the household, domestic abuse, family pressure etc. and other social factors such as: peer pressure involving drug usage; acceptability of drug experimentation in the community; isolation of the individual etc.
- Investigating genetic factors that could lead to addiction. Factors such as density of neurotransmitter receptors in areas in the brain, alteration in brain structures and any genes that if altered could affect the addictive process.
- My investigation methods would be similar to a microscope. firstly I will read books such as "the craving brain" and "the addictive personality" to give me a broad overview of the topic from two perspectives, both biological/physiological (the genetic side of my project) and the emotional/psychological (the environmental side of my project). This will point me in the general direction of factors I should be looking for in both areas, I will then perform a more in depth search using internet sources on factors that could affect addiction to gain a rough understanding of said factor. Then I will specifically search for a reliable source to cite and gain in depth understanding of a factor.

My summary of the comments and advice from my supervisor

It was suggested that my topic was too broad in general, as trying to tackle both the environmental and genetic side of the disorder in such a short report would prevent me from covering either in sufficient detail. I was advised to focus on one aspect, either genetic or environmental only. I was also advised to convert my original project into more of a comparison, as the topic I am investigating will not have a single answer, as the condition is affected by multiple factors, and this type of project would allow for a more comprehensive view of the topic of addiction.

Modifications I have made as a result of my discussion with my supervisor

I have adjusted my current project title based on the advice I received to the following: "to what extent do genetic factors contribute to a propensity towards addiction". I have used the phrase "to what extent" as this allows my study to be comparative and presents the opportunity for critical analysis of each point made, as suggested by my supervisor. Narrowing my project down to just the genetic side of the disorder was based on my judgement that I would be more able to adequately cover the genetic side of the disorder due to my scientific background, and also due to the advice of my supervisor so that I can cover the topic in the correct level of detail. I also removed the idea of focussing on a particular addictive substance as, after a quick browse of potential sources, I realised that this would greatly limit the resources at my disposal, also this allows me to focus on the general addictive process and not the vastly complicated, specific, mechanisms involved with each individual drug/substance.

Date 09 October 2016

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Part A: Candidate proposal

To be completed by the candidate

Working title of my Extended Project.
Present the topic to be researched in the form of a short statement/question/hypothesis with clear focus.
Click here to enter text. To what extent do genetic factors contribute to a propensity towards addiction.

- my initial resources will be

books such as "the craving brain" and any form of journal/article/website I can find online. I will also be using search engines such as infotrack, encyclopaedia Britannica and google scholar.

- the courses of study or area(s) of personal interest to which the topic relates

this course relates to my interest in medicine as a future career. In particular my interest in the brain and its functions, how it operates and the different mechanisms within it, and how these mechanisms are altered by altered gene expression.

- my intended product

I intend to produce a report summarising a comprehensive view of genetic factors that can cause a propensity towards addiction and to what extent these factors are important, with a brief section detailing alternative environmental factors.

Provide details of the courses that you are currently studying

Qualification type	Awarding body & subject
eg A-level, Modern Apprenticeship, BTEC	eg AQA Mathematics, OCR Computing, WJEC English
A-Level	Biology
A-Level	Chemistry
A-Level	Maths

Qualification type	Awarding body & subject
A-Level	Further Maths
Click to enter text.	Click here to enter text.
Click to enter text.	Click here to enter text.
Click to enter text.	Click here to enter text.
Click to enter text.	Click here to enter text.

Notice to candidate You must not take part in any unfair practice in the preparation of project work required for assessment and you must understand that to present material copied directly from any book or any other sources without acknowledgement will be regarded as deliberate deception. If you use or attempt to use any unfair practice you will be reported to AQA and you may be disqualified from all subjects.

Candidate declaration

I certify that I have read and understood AQA's Regulations relating to unfair practice as set out in the notice to candidates above.

signature. Date 09 October 2016

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Part B: Supervisor's comments on candidate proposal

To be completed by the supervisor
Please comment below on the validity and feasibility of the candidate proposal (Part A) as an Extended Project

	Supervisor's comments
Indicate the relation to, and development/extension outside of, the main course(s) of study or interest	Click here to enter text. wish to study medicine next year has encouraged him to develop his interest in Biology and Psychology through further study of the mechanics (biological and, briefly, environmental) of addiction.
Comment on the suitability of the proposed initial sources and research base	Click here to enter text. has a good base for his research and has good local university libraries to broaden his exposure to academic literature.
Confirm that the project is feasible in the proposed timescale and/or indicate any potential difficulties that may prevent the candidate from meeting the assessment objectives	Click here to enter text. This project is broad in scope, but I have confidence in ability to conduct the necessary research to enable him to successfully complete it.

Indicate the expected format of the project product that will be submitted for assessment

☑ Research based written report

☐ Artefact (for example prototype, model, artwork, scientific investigation, creative writing) plus written report

Is the project a contribution to a group exercise? ☐ YES ☑ NO

If Yes, confirm that there is a defined individual contribution by the candidate ☐ YES ☐ NO

List the **other** group members below.

Candidate No. Click. Candidate Name Click here to enter text.

Candidate No. Click. Candidate Name Click here to enter text.

Candidate No. Click. Candidate Name Click here to enter text.

Supervisor signature

Date Click here to enter a date. 18/10/16

Candidate number

Click here to enter.

Candidate's full name

Click here to enter text.

Part C: Centre coordinator's approval of candidate proposal

Supervisor's name

Click here to enter text.

To be completed by the centre coordinator
If you are acting as both the Centre coordinator and the supervisor, please seek counter signature from a senior colleague

Centre coordinator's comments on the feasibility and acceptability of the proposal (parts A & B) as an Extended Project

Click here to enter text.

A broad project with the potential to go into too many areas to keep concise. Make sure you have a clearly defined start to keep it succinct — I'm confident you can do this

☑ Approved

☐ Approved subject to the implementation of the centre coordinator's recommendations

☐ Resubmission required

Centre coordinator's name

Click here to enter text.

Cen

Date 25/5/16

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Planning review

To be completed by the candidate

This page records your outline plan once your proposal has been approved.

My next steps in planning, researching and deadlines that I will set myself. What I intend to do, by when, what resources I will use and how I will implement the recommendations of the centre co-ordinator (where appropriate).

Gain a solid understanding of addiction through reading "the craving brain" and using apps such as 3D-brain to understand more about brain structures in addiction and the different processes within them that can cause the addictive process to begin, deepen or cease. I am hoping to finish this stage of my research by early november.

Using this knowledge, I will attempt to identify different mechanisms that if altered could cause an accelerated descent into addiction, or that could make someone's threshold for becoming addicted lower than usual. I will also be attempting to contact specialists in the subject to discuss certain parts of the process that are particularly intricate and to obtain information on which factors could potentially cause a propensity towards addiction. Using this I will then use the internet and search engines previously listed to find information on these factors firstly for understanding and then secondly identifying a reliable source for the information. During this process, I am hoping to identify other factors on the way and then research these in depth to give a wider range of points. I will then compile all this information into a rough plan outlining all the points I intend to make. I intend to finish this process by early December.

I will collate this information in my report, complete with evaluations of how effective I believe each factor is in causing a propensity towards addiction. I will also attempt to outline some environmental factors which could cause the propensity towards addiction. I am expecting this to be completed by mid-January to early February.

My summary of the comments and advice from my supervisor

Ensure that sources used are reliable, or are at least evaluated for their quality of information. Do not rely solely upon my own identification of factors that could affect the addictive process, as I may not identify some crucial factors, use articles that provide summaries of information on the topic and pick and choose the relevant points to investigate from here. Ensure that the environmental section of my report is equally well sourced and reliable as the genetics section.

Modifications I have made as a result of my discussion with my supervisor and/or the comments from my centre coordinator

to ensure the reliability of sources used, I am attempting to use government or university produced studies for most of my research as these have a certain amount of credibility to them. However, in the absence of such reliable sources I will attempt to use educational sites and failing that I will use less reliable sources but ensure I reference the information across multiple sources to add a certain amount of credibility to them.

I am going to use multiple summary articles on the topic to help me obtain a wider view of the factors I need to consider in my project.

I will also treat the environmental section as seriously as the genetic section in regards to the sourcing of materials and qualification of points made.

Date 16 November 2016

Candidate number Click here to enter.

Candidate's full name Click here to enter text.

Mid-project review

To be completed by the candidate

This page records your outline plan when you have completed your research.

Is my project following my original plan? How has my plan developed?

The original gaining of understanding of addiction took longer than expected and has caused slight delays in my schedule However, I went above and beyond what I intended to originally investigate and this has allowed me to form more complex points in my project. The researching is also taking longer than expected, as I had underestimated the amount of background knowledge required to sufficiently understand certain publications detailing what I need to know for the project. However, once again, going above and beyond where I expected to be allows me to form more logical and complex points in my project. My plan has also altered in that I am keeping the same research methodology, however I am now writing the points as I research them as this allows me to effectively manage my time and keep within the deadlines I have set. This allows me to see how much content each point will provide for my project, and prevent me doing unnecessary research which I may not have time to convert into expanded points in my project, thus allowing me to stick to further deadlines..

My summary of the comments and advice from my supervisor

From what I have written so far, the content has been good, however certain areas of my essays require more qualifying and backing up with suitable evidence. Certain parts of my project also had grammatical errors and unclear messages. It was also identified that the graphs and data sourced from a study was in a rather unfriendly format and was difficult to interpret.

Modifications I have made as a result of my discussion with my supervisor at this stage

I am going to research the discussed areas and attempt to find studies which back up my claims, and ensure they are reliably sourced. I am also going to review each paragraph firstly on my own and then by a family member to ensure that the points made are clear and understandable with no confusion as to what I am conveying I will also take the raw data from the studies I have used and reformat it into an easily interpretable format with clear labelling to prevent confusion along with explanations of what the graph represents alongside the graph.

My final title and agreed form of project product

"To what extent do genetic factors contribute to a propensity towards addiction in humans?" this will be presented in the form of a written paper accompanied by a PowerPoint presentation.

My planned next steps to complete my project

Review what I have so far and ensure points are sufficiently qualified and understandable. I will then proceed to continue identifying factors and writing up points until I feel I have compiled enough evidence to form a weighted conclusion to my project. I am also going to attempt to source more data to qualify my points, so as to make my report more valid.

Date 08 February 2017

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Candidate number Click here to enter.

Candidate's full name Click here to enter text.

Project product review

To be completed by the candidate

This page records the (near) completion of your project product. Outline the successes, failures, additions and/or changes you made as you followed the plan in your mid-project review

Did my project follow my revised plan (from the mid-project review)?

As far as structure of the projects goes my plan was carried out immaculately and it contains all the planned points and more which I came across mid-way through my writing. However as far as deadlines are concerned, I have once again underestimated the time taken for finishing the research and writing for my project. This is because I have come across new information later in my research which I realise could be integral to earlier points and could add a certain depth which would enhance my points. This required restructuring of my essay to include these, however I believe the extension beyond my deadline was justified by the improvements I made to my essay and the extra sources, I found for certain points that felt underqualified, have added an invaluable level of extra reliability to my report. I did have a family member read through my essay and they found it to be understandable in terms of content, however minor adjustments to grammar were suggested. The formatting of my data is now easily interpretable as I tested the graphs on friends and family who found that they could glean the meaning of the graphs even without the context of the surrounding text.

My summary of the comments and advice from my supervisor at this final stage

It would appear that during my writing I had left some points unfinished, as I needed time to think about how to integrate knowledge I had acquired since writing it, and so it caused portions of my essay to be lacking in explanation.

Modifications I have made as a result of discussion with my supervisor at this final stage

Do I need to do anything else to complete my product?

To address this issue I have revisited these areas and ensured that everything is fully qualified and explained.

Date Click here to enter a date.

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Presentation record part A

To be completed by the candidate
This page records your presentation and its preparation.

Planned format of my presentation (eg timing, audience, use of visual aids, slides, use of notes, etc.)
My presentation is planned to be 10 minutes long with a 5 minute section at the end for questions from the audience. My audience will be a group of my peers, other students; my supervisor and assessor, Mr Evans and Mr Moore. I will be using slides with engaging visuals to illustrate my points, as this will help me convey complex ideas in a short period of time. I am avoiding the use of text on my slides, as this will distract from the presentation and with divided attention between me explaining the slide and my audience reading the slide, the message may be lost. My current plan for the presentation is to have a basic sequence of points which I will be addressing in my presentation, and I will have a rough idea of how I will structure each point, although the majority of my speech will be premeditated but improvised. This will allows me to flexible and go into more depth on points that the audience seem to engage with, or to reduce the content of areas which the audience may not engage with, however, I will ensure I do not compromise the content of my presentation by doing so. I will have a page of the sequence of points I will be covering so that if I misremember the sequence, or feel pressured, I have a backup to rely on.

Planned content of my presentation
In my presentation I will address the key parts of my production process and include a brief summary of a few of the more engaging points that best illustrate the conclusion of my report.

From my production process I will be talking about my research methodology, how I initially started my research and built up my knowledge until I felt ready to create coherent points. I will also include a short evaluation, reflecting on my production process and final outcome of the project, including how I would extend and improve my project if given more time and how I would approach the project if I did it again.

For the summary of my report I have included certain select points which I believe are the more interesting and less technical points, which still illustrate both sides of my argument in the report, genetic and environmental. I have done this because I understand that I am pitching to people who do not necessarily have as in depth knowledge on genetics, and the time taken to explain the more complex genetic points I have made in my report would take much longer than the allotted 10 minutes. A specific point I picked were the action of an enzyme involved in nicotine metabolism, as this explained a real life observation, the adverse effects of the initial exposure to nicotine, this application to a real life situation is intended to engage to audience. I also picked 2 other points on neurone polymorphisms and circadian rhythms which are important points that do not require a deep level of understanding. For the environmental factors I have included a multitude of different points which I have then briefly explained as to how they cause a predisposition towards addiction, as this shows the number of different environmental factors that can cause addiction. I do have a section at the end for questions which I feel fully prepared to answer as my research has given me a large area of knowledge which I am capable of adapting to questions.

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

Modifications I have made as a result of rehearsal and/or discussion with my supervisor

After my rehearsal I was told that my sequence of slides felt slightly disordered and hard to follow in sequence, following this I decided to reorganise my presentation so that I first addressed the content of my report and then afterwards addressed my production process and evaluated my project. I was also told that in some areas I didn't explain enough of the background science that qualifies my points. Reflecting on this I decided to add a slide which explained the basic premise of what a mutation is, this should provide all the relevant knowledge of genetics required to understand the points I make later in the presentation. As far as the delivery of my presentation is concerned I was told that whilst my body language and engagement was good, I was talking too fast, and so in my actual presentation I will make a conscious effort to speak clearly and with appropriate speed. I was also told that my evaluation section could be more extensive and so I have added a considerable section to this portion of my presentation.

AO3
L.III
Demonstrate development/evaluation of project, planning.

Date 14 March 2017

Candidate number	Candidate's full name

Presentation record part B

To be completed by the supervisor
Record and comment below on the delivery of the presentation

	Supervisor's record/comments
The nature of the audience (include numbers of staff, students and others present)	4 students 2 staff
The nature of the presentation (include use of notes, use of display items, and use of presentation software)	ppt ... Ben spoke without a script.
Comment on the content and delivery of the presentation (for example clarity of ideas, structure of presentation, pace, engagement with audience)	clarity of ideas was v. good excellent clarity. pace + engagement with audience was excellent Presentation clearly well structured and delivered confidently
Comment on the response of the candidate to questions that demonstrated understanding and grasp of the project and/or its production. **Give examples of questions asked and answers given.**	In terms of production of artifact: - see over ⇒

Supervisor signature

Date 15/3/17.

3D Eni

→ Ethical pre-treatment identification of those likely to be addicted?
Controversial? – given that it is hard to separate ↑

— really good area to this Ben should a clear awareness of the potential implications of this case data and illustrated good synthesis of a like range of sites.

- Which research were not included? – Clear awareness of
- An addict? perseverance & research used
- Count? relative reliability thereafter

→ Detailed article appraisal here. Ability to reflect analytically and critically on the whole process.

Candidate number Click here to enter.

Candidate's full name Click here to enter text.

Presentation record part B

To be completed by the supervisor
Record and comment below on the delivery of the presentation

	Supervisor's record/comments
The nature of the audience (include numbers of staff, students and others present)	Click here to enter text.
The nature of the presentation (include use of notes, use of display items, and use of presentation software)	Click here to enter text.
Comment on the content and delivery of the presentation (for example clarity of ideas, structure of presentation, pace, engagement with audience)	Click here to enter text.
Comment on the response of the candidate to questions that demonstrated understanding and grasp of the project and/or its production. **Give examples of questions asked and answers given.**	Click here to enter text.

Supervisor signature.

Date Click here to enter a date.

Candidate number	Candidate's full name
Click here to enter.	Click here to enter text.

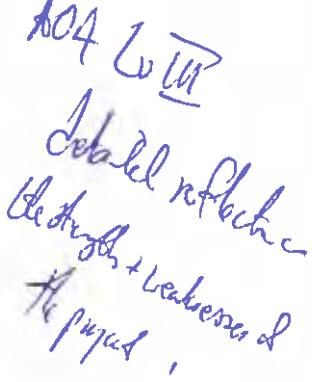
Summary and reflection

To be completed by the candidate
This page records your summary, reflection and evaluation when you have completed your project product and given your presentation.

Some questions you may wish to answer in this section include, what have I learned from completing this project? What new knowledge or expertise have I enjoyed or found valuable? What are the strengths and weaknesses of my project (including planning and organisation)? What skills have I improved? What changes would I make if I undertook such work again? What advice would I give to others undertaking such a project?

From completing the EPQ project I have developed many skills such as my research methodology. Throughout the process my approach at gathering information has altered, from searching directly for specific points to put into my report, which is flawed as it provides only a limited view of the topic, to a more developed extensive method of researching. The more developed method involved firstly briefly researched the entire topic to gain an understanding of the general process I was investigating and then from this researching specific points that I highlighted as important. An example being reading books on the process of addiction which then led me to independently identify genetic factors that had potential to cause a predisposition towards addiction, such as disruption of circadian rhythms. This method of research is better as it allowed me to provide a more comprehensive summary of the topic as I had a greater understanding and so could make the relevant judgements necessary for assessing the role of genetic factors in a propensity towards addiction. I have learnt how to correctly reference sources using the Harvard referencing system, which will be a useful skill that I can apply to later life. I have developed my critical analysis skills involved in assessing the credibility of sources and how this affects the reliability of my report. For example, for most of my sources I did further research after selecting a source to see if there were other sources which verify the information I used, thus reducing the risk that I was using unreliable information in my report. I also very much enjoyed learning about the biological and neurological processes involved in the development of addiction, in particular learning how brain structures related to their individual functions. Another area was the knowledge of the complex mechanisms within addiction, how it was not just a single factor, but many factors that interacted with each other to produce the end phenotype. I believe a strength of my project was the personal interest I have in the topic which drove me to research beyond what I would put into my project, as this larger field of knowledge on the topic allowed me to produce a more in depth informed report. Another strength with my research was the breadth of sources I used, this vast quantity of information allowed me to select only the genetic factors which I believed were the most significant in causing a predisposition towards addiction. However a weakness with my project and research was the broadness of the topic chosen. Whilst it gave me a large amount of data and information to work with, a large portion of it was inconsequential to my project and meant that there was a great deal of critical selection of only the best pieces of information. Having to sift through the literature on the topic at hand meant that I ran over my deadline for research which is regrettable; however I regained some of this time by writing and researching at the same time. Throughout my project deadlines were a difficulty due to an underestimation of the amount of literature I would find on my research topic, but in my planning I had left time spare after my deadlines before the project was due so that if any task overran it would not affect the deadline for handing in my project. I believe on of the greatest successes of my planning was the rough structure of my project I laid out as this guided my research and writing to help me produce a comprehensive report. One of the strengths of my project is that it is sourced, for the large part, from scientific studies performed with large sample sizes and by reputable organisations, this allows me to be fairly confident that the points I have made are valid and qualified. However in part my project was the assessment of to what extent each factor in particular caused the predisposition towards addiction, and this assessment was a qualitative assessment formed from my own opinions. This means that any assessments made were based on my knowledge and research alone, this leaves some degree of uncertainty of the truth of the matter when it comes to my conclusions. However I believe that using the limited information available I have made a reasonable conclusion, and due to the inseparable nature of genetic and environmental factors, there is no clear answer which I have adequately reflected in my conclusion. Another strength of my project is the combination of breadth, in the form of an overview of the topic, and depth, in the form of specific genetic factors, it includes, as this allows for a more comprehensive answer and conclusion to my initial question. The breadth in question is the evidence of genetic factors acting together to produce an addictive phenotype, as shown by the twin studies. Along with the depth, in demonstrating the individual cases in which genetic factors act, such as the dysfunctional CYP2A6 enzyme. However tied into this success is a weakness, in that the topic I attempted to tackle is larger than could be adequately summed up in such a short project, and so it is a combination of breadth and depth that best summarises the vast amounts of literature on the subject. If I had much more time and greater access to resources I could provide a report which is consistently in depth and

covers the entirety of the current literature. Or if it were still under the same circumstance I could attempt to pick one particular set of genetic factors that cause a predisposition towards addiction and specifically investigate how they interact with one another, thus allowing for a detailed and comprehensive report on a smaller topic. A particular weakness of my project is that it doesn't adequately address the other side of the predisposition towards addiction, environmental factors. Due to my specific knowledge and experience in biology and chemistry I geared my project towards my expertise and focussed on the genetic aspect of the disorder and in doing so made a necessary sacrifice to the time and effort I could use exploring the environmental side of the disorder. Whilst this allowed me to provide a more in depth view of genetic factors, which is what my report was intended to address, it leaves a level of uncertainty to the conclusions I have made. If I were to do this again, I could perhaps change my title to include environmental factors as well and research the effects and combinations of the two sides of the disorder so as to reach more comprehensive conclusions to my question. If I were advising anyone undertaking the epq project I would advise them to do some preliminary research into their question to see if the topic is too broad or doesn't have enough literature etc. as this would allow them to rule out possible questions or topics which may be too difficult to undertake. I would also advise that it is never to early or too late to be researching, as I found that researching throughout the project allows you to return to certain ideas or areas of research after having time to think about the particular source, this allows you to reflect on your project all the way through. I would advise them to rigorously stick to their self-set deadlines, and ensure there is time left for unexpected delays, as this allows you extend research or writing if a new idea strikes you that you feel may be important to your project.



TO WHAT EXTENT DO GENETIC FACTORS CONTRIBUTE TO A PROPENSITY TOWARDS ADDICTION IN HUMANS?

FEBRUARY 22, 2017

Contents

Glossary

- Neurotransmitter- chemicals in the brain responsible for communication between brain cells
- Dopamine- a neurotransmitter for communicating within the brain, strong role in motivation and reward circuits
- Genome- the complete set of genes of an individual
- Phenotype- observable characteristics of an individual, based upon the interaction between their genes and environment
- Serotonin- a neurotransmitter for communicating within the brain, strong role in providing a feeling of satiation
- Metabolite- a chemical or substance involved in the metabolism, formation and break down, breakdown
- Dopaminergic pathways- pathways in the brain that use dopamine as their neurotransmitter, usually associated with areas of the brain involved in reward and motivation
- Mesocorticolimbic pathway- a pathway of neurones in the brain that leads through, and can activate, multiple areas in the brain associated with reward
- Precursor molecule- a substance from which another substance is formed
- Allelic frequency- the prevalence of a particular allele within a population
- Antagonist- a substance which interferes or inhibits the physiological action of another
- Phosphorylation- the introduction of a phosphate molecule

- Stressor- the thing that is causing stress

The above definitions were sourced from oxford online dictionary, with supplementary information added in some cases.

Introduction

In this project I will be investigating the different genetic factors that can cause an individual to have a greater likelihood of becoming addicted. I will be investigating areas such as the different neurotransmitters involved in the brain during the addictive process, neurones involved in the addictive process and in particular different variations of genes, polymorphisms, which can cause different effects in areas crucial to the addictive process. I will also be analysing some non-genetic factors (environmental factors) which could have an effect on someone's propensity towards addiction.

Firstly I must establish what it is that I mean by addiction. Addiction has many different definitions depending on the organisation describing it. Whether it is the DSM[1], a diagnostic manual developed for psychiatrists, or the American society of addictive medicine (ASAM)[2], for the use of describing the illness itself. However whilst they all differ they commonly state that it is a psychiatric disorder involving the compulsive use and abuse of an addictive substance or behaviour that ultimately results in physical and psychological trauma[3]. For the purpose of this project I'm going to subject my definition of addiction to certain simplifications to avoid confusion, I will be focussing on specific physiological aspects of the disorder.

Overview of observable effects of genetic influence on addiction

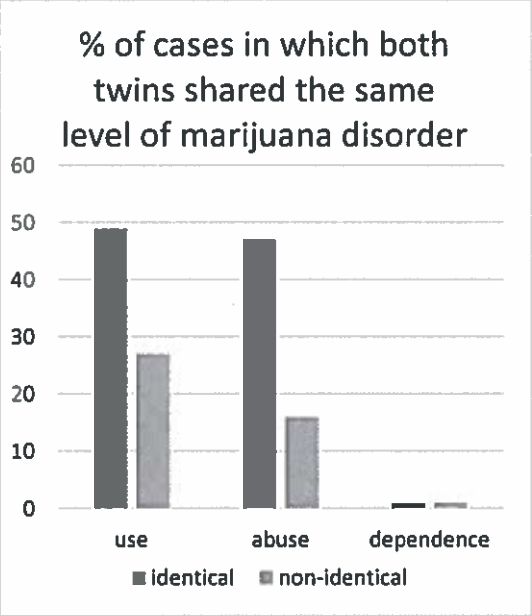
Twin studies

Twin studies are a useful method for investigating the effect of genetics on individuals as it allows you to observe the strength of genetic influence over a trait. This is because any identical twins will have the same genetics and so if a trait is genetically controlled, it will be common to both twins. Whereas non identical twins act as a control group, as they are siblings with the most similar environment (the same as with identical twins), however they have different genetics. Therefore a comparison between the two results from identical twins and non-identical twins will show to what extent a trait is genetically controlled.

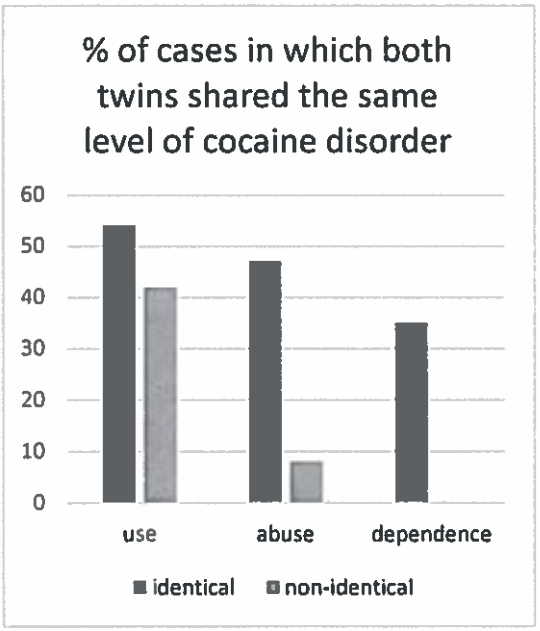
An example of this would be Dr. Kenneth Kendler and Dr. Carol Prescott's experiment[4] in which they assessed 1934 female twins, both identical and non-identical, for their use, abuse or dependence on marijuana or cocaine. In this study they recorded the concordance between twins, whether both twins had the same level of disorder, e.g. if both had used, both had abused or both had a

[1] (American Psychiatric Association, 2017)
[2] (medicine, American society of addiction, 2016)
[3] (National institute on drug abuse, 2017)
[4] (Zickler, 1999)

dependence on the substance. The results from the experiment are represented in the following graphs. In this study the categories of use, abuse and dependence can be found on the study[4].



These graphs[4] can be interpreted to show that there is a strong genetic factor that leads towards abuse of marijuana and cocaine. This is demonstrated by how in the abuse category the percentage of concordance amongst twins for both cocaine and marijuana is much greater amongst the identical twins when compared to the non-identical twins. This is significant because if a trait is controlled more by the genetics of the individual then you would expect two people with identical genomes, identical twins, to exhibit the same trait. Whereas if the two individuals didn't have identical genomes, non-identical twins, it would be less likely that both would exhibit the same trait as they are less likely to both have the same particular genetic variation that causes the trait.



As shown by these graphs this is the exact case for use and abuse of marijuana or cocaine, in that concordance is consistently higher amongst the identical twins, thus showing that genetics play a heavy role in abuse of substances as part of addiction.

Another important feature of this graph is the remarkably high percentage concordance of cocaine dependence in identical twins. The fact that there were no incidences of both fraternal twins being cocaine dependant and yet there is a 35% concordance amongst identical twins shows that there must be a very heavy genetic influence upon developing dependence on highly addictive substances such as cocaine.

If we consider just the cocaine results amongst non-identical twins, you can see a large decline in concordance from use to abuse and then to no cases of concordant dependence. Whereas with identical twins there is a much smaller decrease in concordance between use, abuse and dependence until there is a very large difference between the two sets of results. I can speculate that this divergence of results is due to a change in the relative influence of environmental and genetic factors between the categories of use, abuse and dependence. In short I speculate that as the substance use/abuse continues and escalates into drug dependence, the genetics of the individual become more prevalent in the response of the individual, therefore at the climax of the substance abuse disorder, addiction, genetic factors are more prevalent in the disorder.

Genetic lineage and addiction in rats

There is a definite correlation between the genetics of the individual and their likelihood of becoming addicted to a substance or behaviour as shown by the T. K. Li et al's experiment[5], in 1989, involving the selective breeding of rats to produce offspring with a definite preference for alcohol. This occurred through the selective breeding of rats that had shown a natural tendency to alcohol together, and then the offspring would breed with other alcohol preferring rats to further refine a genome showed and expressed phenotype with a clear preference for alcohol. In this experiment the alcohol preferring rats were compared against a line of rats selectively bred to not prefer alcohol, these were assumedly selectively bred using the same methods. The mere fact that this can be done shows that, through genetic input alone, a propensity towards the use of substances can be formed, and therefore that the genome of the individual plays an extremely important role in propensity towards developing addiction. It can be assumed that in a professional experiment done by such high calibre scientists that the conditions were highly controlled and that there was minimal difference in the environmental conditions of the different rats, so as to provide the best representation of solely the genetic factors at play here. As if the environmental factors are identical for every rat then they can be considered negligible in their effect on the results, thus allowing the results for alcohol preferring and non-alcohol preferring rats to be directly compared to analyse the difference caused by the difference in phenotypes. Furthermore the experiment is made more credible by the fact that after the experiment a second line of alcohol preferring rats was bred, showing the repeatability of the results.

In this experiment they also analysed the concentrations of key chemicals in the brains of each line of rats and in their comparison they noted that there was a 10-20% lower concentration of serotonin and its metabolite 5-hydroxyindoleatic acid in areas of the brain such as the cerebral cortex, striatum, nucleus accumbens, the hypothalamus and the hippocampus. With a less than 0.05 probability that these results are down to chance it can be assumed that these results are reliable. The fact that these areas have a lower concentration of serotonin shows that they will be more sensitised to the stimulating action of dopamine, meaning they will more readily make connections within the brain. This coupled with the significance of the functions of these areas of the brain show that this genetically low concentration of serotonin can cause a predisposition towards addiction.

The cerebral cortex is the area of the brain most associated with higher brain function, showing that our cognition in response to addictive substances is affected by our genetics; the striatum is a nucleus within the basal ganglia responsible for selecting the appropriate action to achieve a goal[6] and so would be the coordinator of actions to help attain the addictive substance or behaviour; the nucleus accumbens, another nucleus within the basal ganglia responsible for rewarding behaviour, which when sensitised by low serotonin levels will release dopamine to increase the motivation of the organism to seek out addictive behaviour; the hippocampus and hypothalamus will together reinforce the behaviour by committing information such as the positive memory of using the drug and the negative memory of drug withdrawal to memory so as to reinforce the addictive behaviour of the organism in seeking out the addictive substance and then ensuring the usage is continued[7,8].

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[5] (McBride WJ, 2013)
[6] (unknown, 2015)*
[7] (DNA Learning Center, 2017)
[8] (unknown, 2015)*

In short through only genetic influence a perfect addictive neural landscape has been formed, to the extent that the smallest influence from any outside stimulus would tip an individual, with this neural composition, towards addiction.

The shortcomings of the experiment come in the fact that this experiment was performed on rats and there are undoubtedly differences in the brain structures or rats and humans. However the areas affected as described above are mostly in the more primal areas of the brain, with the exception of the cerebral cortex. By this I mean that due to evolutionary pathways the structures in the primal brain and their functions differ very little as they are key to survival mechanisms common to all mammals[9]. Therefore it can be safely assumed that interactions in these areas of the brain would differ very little from rats to humans. However the cerebral cortex is one of the key differences between humans and other mammals, in humans the cerebral cortex is much more developed and perhaps could have a stronger influence over the body than the primal mechanisms when compared to mammals with less a developed cerebral cortex e.g. rats. So there is some limit to the relatability of this information to humans. Also whilst this experiment does prove that a genetic composition can be achieved that causes a strong predisposition towards addiction, this was obtained from a long line of selective breeding, which it's safe to say is incredibly unlikely to occur in a human population. So it is unlikely that a person with this "perfect" addictive setup would ever be born. However it is arguable that as addiction is so all consuming its most likely that the only people addicts really come into contact with or connect with will be people who are involved in their addictive cycle and who are possibly also addicts. This lends credibility to the idea that environmental circumstances could give rise to a person with genetics geared more towards becoming addicted.

A similar experiment[10] was conducted in 1993 involving the experimentation on lines of both alcohol preferring and non-alcohol preferring rats in which dopamine release in the brain was monitored after self-administration of different concentrations of alcohol and then compared against the baseline dopamine levels of the individual. In this experiment it was observed that after oral alcohol consumption of the same concentration the alcohol preferring rats dopamine levels increased from baseline to between 143-459% of the baseline level whereas in non-alcohol preferring rats the increase ranged from only 142-212%. These results show that there is most definitely genetic variation in the amount of dopamine released as a reward upon the reception of the same stimulus between organisms. This supports the idea that some people gain more pleasure from the use of addictive substances than others which leads to the assessment that some people could be more motivated towards addiction than others. Whether this reward is stronger in alcohol preferring rats due to purely genetics can be brought into question as the alcohol preferring rats may have higher dopamine release due to operant conditioning[11]. This is because if they are used to exposure to alcohol and have learnt to expect alcohol and so the nucleus accumbens releases dopamine to stimulate the action to obtain the alcohol, thus further increasing dopamine levels, whereas the non-alcohol preferring rats wouldn't have this pre-existing conditioning and wouldn't release dopamine at this time. However the fact that within both groups there is a wide range of variation shows that there is some form of genetic factor that affects reward received upon stimulation. This

[9] (Genetic science learning center, 2013)
[10] (Department of Neuropharmacology, Scripps Research Institute, La Jolla, California., 1993)
[11] (Kalivas, 2009)*

can once again be extrapolated to a human level because the reward system involved in this experiment is universal to all mammals as it was a primal survival system. This fully supports the idea that there are genetic factors that lead towards a propensity towards addiction.

Genetic factors affecting cellular and molecular mechanisms in addiction

Now that I have shown the overview that there is definitely some form of genetic influence over predisposition towards addiction, I am going to deepen my search to attempt to identify some possible causes for the predisposition. This will involve searching at a deeper level in terms of neurotransmitters, their receptors, brain structures and their polymorphisms.

Polymorphisms in dopaminergic pathways

During rewarding behaviour dopamine is transmitted through the brain via a multitude of neurone pathways, called dopaminergic pathways, this provides a sensation of pleasure[12,13]. In a system where perhaps the dopaminergic pathways aren't as effective at rewarding behaviour, the individual may be stimulated to seek out greater or more frequent pleasures, such as those that come from addictive substances or overuse of a substance or behaviour. This is demonstrated by a review from the University of California[14], in which they analyse the effects of the polymorphisms of the Dopamine receptor gene (referred to as DRD2) on addiction. From this they concluded that the specific A1 allele of the gene renders the dopaminergic pathways in the brain inefficient, and can cause the individual to seek out substances or activities which activate the mesocorticolimbic pathways and provide the necessary dopamine for their satisfaction. The A1 allele seems to have two effects: firstly it decreases the D2 dopamine receptor density on the striatum, a part of the brain involved in reward cognition[15]. This would result in a lesser feeling of reward from behaviour that would usually be rewarding, thus causing the person to seek out highly rewarding or repeating rewarding behaviour, exactly as found in addictive behaviour. However, the second effect of the A1 allele is that in the body's attempt to counteract the ineffective reward system there is a higher level of activity of the enzyme aromatic L-amino acid decarboxylase in the striatum (Department of Pharmacology and Clinical Pharmacology, University of Turku, 2005). Aromatic L-amino acid decarboxylase is an enzyme which converts the dopamine precursor L-DOPA into dopamine, this means that the body has attempted to compensate for the lack of dopamine sensitivity by increasing the levels of dopamine in the deficient areas.

So in this case it becomes a question of which is more prevalent, the lower receptor density in causing reward cravings or the body's counter mechanism in trying to supply a higher sensation of reward for more mundane actions. I have found that the allelic frequency of the A1 allele is 0.2 in a British Caucasian population[16] and whilst this is rather high the allele could be recessive or be masked by another gene through epistasis to cause it to not be expressed. It is incredibly hard to define how much of an effect this would have on an individual as there are so many other factors which could affect the persons behaviour. However I would speculate that this gene, in causing

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[12] (Robbins, n.d.)
[13] (Robbins, n.d.)
[14] (EP, 2000)
[15] (unknown, 2015)*
[16] (Department of Psychiatry and Behavioural Sciences, University College London Medical School, 1997)

people to seek out highly rewarding activity, is a very important factor in the beginning of an addiction as it pushes the individual towards addictive behaviour or substances.

Autoreceptors

Autoreceptors are a specific type of receptor which can be located on D2 type neurones where they regulate both release of dopamine by the presynaptic neurone and the sensitivity of the postsynaptic neurone to dopamine. There was a study in which they removed the gene coding for the Autoreceptors in mice which an interesting effect. The mice appeared hyperactive and had a largely increased sensitivity towards addictive substances such as cocaine. This is due to the increase in synthesis and release of dopamine in response to stimuli, which produces a neural landscape which is highly motivated towards seeking addictive behaviour and responds in a highly rewarding manner to such stimuli. This is ideal circumstances for the formation of addictive behaviour. These results were obtained in an experiment in which the gene was removed entirely, which would be impossible in any realistic circumstance, and so this example couldn't occur in humans. However, it could be extrapolated to some extent perhaps to a person in which perhaps there was a defect in the AUTODRD2 gene that causes the Autoreceptors to perhaps not respond as effectively to the release of dopamine, so that the sensitivity of the post synaptic neurone and the quantity of dopamine released doesn't decrease and a similar effect as was produced in the mice could be achieved. Therefore, a mutation in the Autoreceptors on D2 type neurones has potential to cause a significant propensity towards addiction.

Transcription factors

A very prevalent factor in controlling propensity towards addiction is transcription factors. These are groups of proteins that control the expression of certain genes, they can increase or decrease the production of certain proteins and can have profound effects within the areas in which they act. When an individual performs their addictive activity and the brain is flooded with high levels of dopamine, many dopamine receptors are activated in the nucleus accumbens and ventral tegmental area. This causes increased phosphorylation of a transcription factor CREB thus inhibiting its function as a transcription factor, this has 2 important effects in the addictive process[17,18,19]

Firstly it inhibits the production of tyrosine hydroxylase, which is significant because this is an enzyme involved in the process of dopamine production, and a lack of this enzyme has been associated with low dopamine levels. This reduces the reward received from everyday activities that would otherwise provide reward and satiation and causes the individual to seek out highly rewarding activities, e.g. addictive substances.

Secondly it inhibits the production of ΔJun, an antagonist of ΔFosB (another transcription factor), this allows for the overexpression of ΔFosB as it is no longer inhibited. ΔFosB performs many functions, but the function most relevant is its ability to increase the sensitisation to certain stimuli, thus creating a greater reward from addictive substances and encouraging addictive behaviour. It does this through stimulating the production of brain derived neurotrophic factor (BDNF) in the nucleus accumbens, this causes new neurones to form between the nucleus accumbens and the

[17] (unknown, 2016)
[18] (Eric J. Nestler, 2001)
[19] (Renthal W, 2008)

prefrontal cortex allowing for sentient links to be made between the use of an addictive substance and its reward.

Within this sequence of events there are several things that have been identified which could lead to a greater propensity towards addiction. Firstly, a mutation in the gene coding for CREB could produce ineffective CREB proteins which would then not perform as efficiently and have the same effect as having partial inhibition of the CREB transcription factor, thus contributing towards a propensity towards addiction. This is demonstrated by a study in India[20] which identifies several small changes in the DNA, in the gene coding for CREB, which were shown to contribute towards addiction. This was shown by the significantly higher frequency of the polymorphism amongst both alcoholics and opioid dependant individuals when compared to control subjects. The results of this experiment can be assumed to be reliable as the probability that the observed pattern was due to chance was less than 0.0011 when comparing the genotypes of the alcoholics and the control samples and then less than 0.0001 when comparing the genotypes of the opioid dependent individuals and control samples. The limitations of this study is in its selective sampling, in that it was a study of only males Bengali-Hindi ethnicity from Kolkata, and so may not show an accurate representation of the frequency of this mutation and its effects in other geographical populations or in the female biological gender. However, the sample size of this experiment was relatively large and so the results can be considered accurate for this particular population.

Secondly I would identify that if there were increased baseline levels of BDNF in the reward centres of the brain it would be more susceptible to forming new neurones associated with highly rewarding activities and would drive substance abuse or other addictive activities. A study demonstrating the effect of polymorphisms in the BDNF gene[21], rs6265, shows that the c allele in particular causes a propensity towards methamphetamine dependence in a south Asian population, with a probability of less than 0.004 that the results were down to chance. Whilst this study used a large amount of secondary data, it was taken from a specific populous, south Asia and China, and so may not be applicable to populations elsewhere. Another fact to consider in the reliability of this study is that it took data on addicts of different substances e.g. methamphetamine, heroin, nicotine, alcohol, and yet there was only found to be a significant effect, of the c allele, in those with a methamphetamine addiction in south Asia. These results however had a 0.004 probability that the results were down to chance and so can be considered to be very reliable. Although it does bring into question whether polymorphisms in this gene can only contribute towards a propensity to certain substance addictions. However, the study also showed that different combinations of different polymorphisms of the gene had been showed to form propensities towards other addictive substances, such as heroin dependency in Chinese populations. This leads me to assume that there could be certain combinations of alleles that can cause greater or lesser propensities towards addiction of a substance, and that they may not have been observed in these studies as the effects of the polymorphism were less observable with less addictive substances, such as nicotine and alcohol, than with the more addictive substances, such as heroin and methamphetamine.

[20] (Indian Institute of Chemical Biology, 2011)
[21] (Haerian, 2013)

Circadian rhythms

A circadian rhythm is a roughly 24 hour cycle, determined by our internal body clock, of processes within the body and they are vital in maintaining healthy physiological and psychological function. Disruption of these rhythms can have adverse effects on neurological processes such as the release of important neurotransmitters such as dopamine.

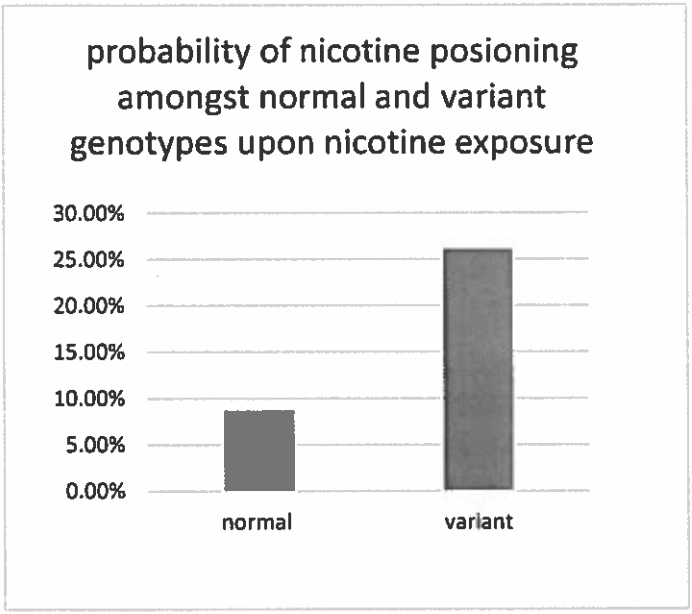
An example of this is a study[22] in which a set of mice were genetically engineered to have altered clock genes, the genes that control the circadian rhythms and body clock, and were then exposed to cocaine and compared to a control group of mice with normal clock genes which were also exposed to cocaine. The results showed that the mice with the variant genes appeared to have higher baseline levels of dopamine and received greater increases in the amount of dopamine released upon exposure to cocaine, when compared to the regular mice. This means that the mice would have a greater drive to attain the addictive substance and receive a greater reward upon administration of the addictive substance. The mice also showed peculiar behaviour in that they remained in the site of cocaine administration and ignored the rewards presented by other rewarding activities in favour of cocaine, even when the cocaine wasn't available. This is classic addictive behaviour of forsaking other sources of pleasure for addictive behaviour. These results show that mice with this variant clock gene are much more susceptible to becoming addicted to a substance from a lesser level of exposure. This study is further supported by a second study[23] which investigated the effect of a mutation on another clock gene in mice, the results showed that the mice were more prone to consuming large quantities of alcohol and that their rate of metabolism of alcohol was reduced. This shows that disruption of the clock genes controlling circadian rhythms can cause addictive behaviour and a greater susceptibility to addictive substances, a potent mix when considering propensity towards addiction. However in these experiments the mice were bred to have mutant variations of clock genes and in humans it is unlikely that such a severe mutation would be found naturally, but perhaps a more minor mutation could cause a partially defective clock gene which may have reduced effects. Overall it is hard to determine to what extent this factor would have an effect however I would suggest that it has potential to cause a strong propensity towards addiction.

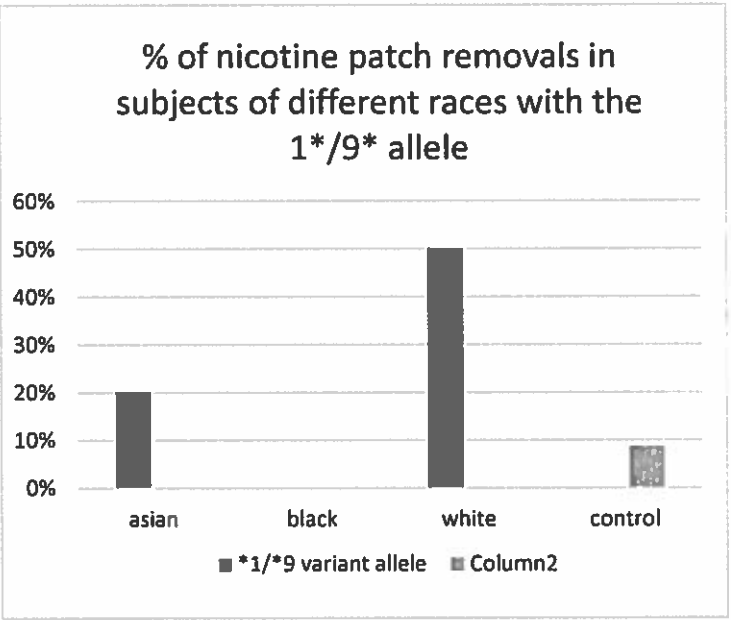
Deterrent genes

Due to their genetic makeup, some individuals may feel less of a rush after taking an addictive substance and some may even have adverse effects such as nausea, which could decrease a person's susceptibility towards experimenting with or becoming dependent on a substance. An example of this would be smoking, Smokers with a certain polymorphism of the CYP2A6 gene feel nausea and dizziness to varying degrees after nicotine administration. This is most likely because the CYP2A6 enzyme is responsible, in part, for the metabolism of nicotine[24]. Therefore, those with defective CYP2A6 genes cannot metabolise nicotine as efficiently, and therefore suffer from nicotine poisoning, which would most definitely be a deterrent to a person smoking and becoming addicted to nicotine.

[22] (UT Southwestern Medical Center, 2005)
[23] (Green, unknown)
[24] (Centre for Addictions and Mental Health, 2001)

However, as this study by the University of California demonstrates[25], different variations in the CYP2A6 gene have different reactions. This study exposed a number of subjects, who had never smoked, to 7mg nicotine patches and observed the effects on the individual until an 8-hour period had passed or the effects of the nicotine poisoning became severe enough for the patch to be removed. From the results obtained, 3 out of the 35 individuals with the wild (natural) allele of the CYP2A6 gene had to remove the nicotine patch, this acted as the control sample. In comparison to this control sample one variant genotype stood out as having a profoundly higher number of individuals removing the nicotine patch within the 8-hour period, the *1/*9 combination of alleles, with 3 out of 9 subjects removing the nicotine patch. This is a 288% increase in the number of people removing the patch when compared to the control sample. Whilst this is a relatively small sample, it is sufficiently large to show that there is a clear difference in the nauseating and dizzying effects of nicotine upon individuals of this genotype when compared to the control sample.





Another notable factor here is the race of the test subjects, in that this particular variant genotype was only present in white and Asian populations and that in white populations it had a greater effect on the subjects and more people removed the patch. This could suggest two things, that this genotypic frequency is higher in certain ethnicities, or that this variant genotype has different effects depending on the ethnicity of the individual. Furthermore, as some of the previous studies can back up, certain alleles can have a different effects in different ethnic groups. For example the c allele of the CREB gene appeared to only have notable effects in propensity towards methamphetamine dependence in south Asia and this variant allele for CYP2A6 appears to be more common amongst Asian populations but more effective in white populations.

Whilst there were certain genotypes with a 50%-100% removal rate of the patch, I deemed these unreliable as the sample size for people with these genotypes was 1 or 2 subjects and so can't be reliably extrapolated to a larger population.

As far as the prevention of development of addiction is concerned I would say this could act as a preventative, as a negative first experience of an addictive drug or behaviour could deter them from

[25] (DA Dempsey, 2013)

further use. However if the other factors pushing them towards addiction were great enough I do not think this will be a strong enough deterrent to prevent repeated exposure. Therefore I would rate this as a minor factor in causing a propensity towards addiction.

Co-morbidity of disorders

There is strong evidence to support the idea that certain mental disorders can lead to the formation of addiction and form a co-morbidity, the presence of multiple disorders/diseases which interact with each other to affect the course of the disorders/diseases. As with many conditions, if you are susceptible to one specific condition, there is a chance you will also be susceptible to related conditions.

There has been strong evidence to suggest that depression is an illness that can lead to a propensity towards addiction. This is because during times of severe depression people may develop coping mechanisms, which could be mundane or illicit, and they can easily turn from a coping mechanism to an addictive ritual they need to fulfil to cope, to either bring them pleasure or to numb emotional pain. Other mental disorders such as panic disorders and social anxiety have been linked to substance abuse disorder as precursors, as they put a great deal of emotional strain upon the individual which could push them towards unhealthy coping mechanisms such as addiction. All of these disorders have, in their own right, been shown to have moderate or strong genetic roots and heritability[26,27,28,29]. This means that every genetic factor that leads to a propensity towards these disorders could in turn lead to this comorbidity of disorders and addiction.

Although these disorders could potentially lead to comorbidity so severe that the substance abuse turns into full blown addiction, there would need to be very specific circumstances to first of all produce the severe case of depression, anxiety disorder or panic disorder. This leads me to believe that whilst this can be a prevalent factor in some cases, in the vast majority of cases this would not be as much of a prevalent factor in causing a propensity towards addiction.

In any case, there would need to be a strong environmental factor to first of all trigger the initial disorder of depression, anxiety or panic, before it could become severe enough to produce comorbidity. There are also certain disorders, such as PTSD, caused by environmental factors, which are strongly linked to comorbidity with substance abuse, thus, supporting the prevalence of environmental factors in causing a propensity towards addiction.

Non-genetic factors

Whilst the majority of this project is dedicated to genetic factors that contribute towards a propensity towards addiction, addiction is a complex disorder with countless contributing factors. Other factors that cause a propensity towards addiction would have to come from the environment and lifestyle of the individual. These factors can include anything from childhood trauma and dysfunctional parental relationships to community poverty and drug availability.

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[26] (Hae-Ran Na, 2011)
[27] (Douglas F. Levinson, n.d.)
[28] (Morris-Rosendahl, 2002)
[29] (Lohoff, 2010)

Stress, stressors and addiction

It's no surprise that stress is the non-genetic factor that causes the greatest impact on propensity towards addiction[30], as stress is a state of discomfort that we are biologically compelled to avoid by any means necessary, if the stress is severe enough. Stress can come in many different forms in anything from social pressures, such as work or family problems, to more evolutionary stresses such as hunger and fear. The effect of stress on your body is a reduction in serotonin and an increase in dopamine production, in this circumstance it causes the urge to remove the source of stress, whether that is to finish the assignment due in tomorrow or to eat to satiate your hunger. This is the logical method for removing the stressor and will provide satiation and remove the stress.

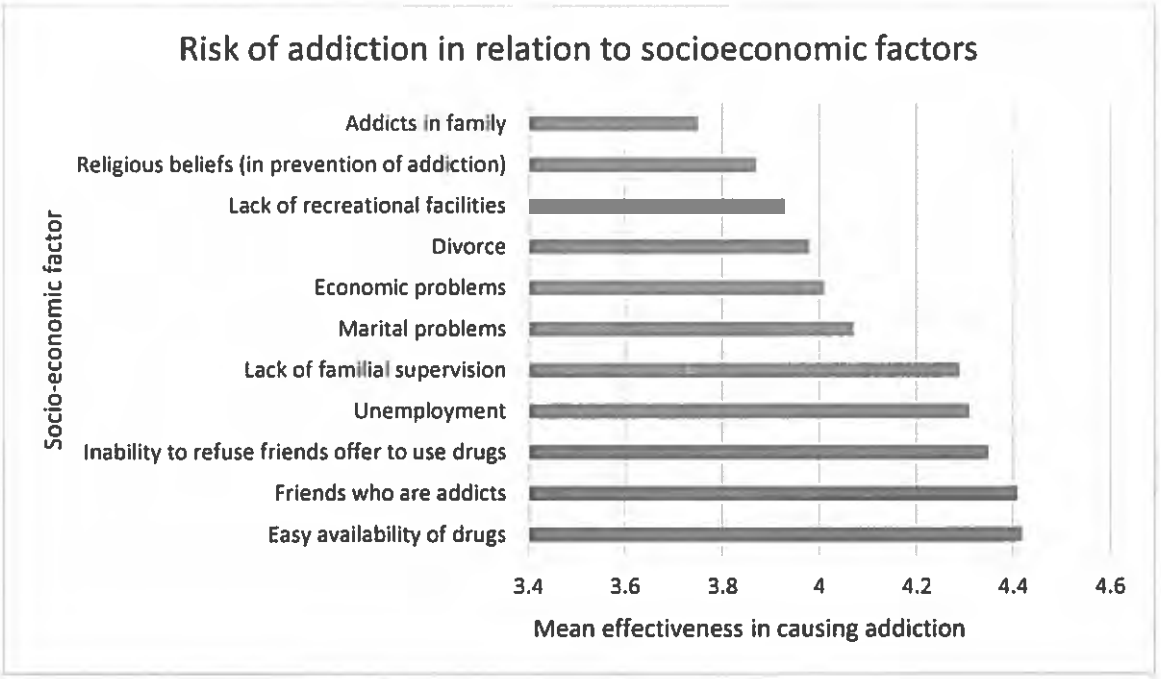
However, the use of addictive behaviour can be used to bypass the stressor to provide satiation. For example, when stressed, some people choose to eat, this will provide satiation of a different kind and will satisfy the body's needs for a while but once the serotonin lowers once again the stress will return and a greater satiation will be required to overcome the stressor. The greater the stress, the greater the reward needed to overcome the stress. Therefore, in examples of chronic inescapable stress, where the stressor can't be removed, some people turn to the use of highly rewarding addictive substances or behaviours to provide satiation without removing the stressor, and this is why high stress levels can turn people towards addictive behaviour[31].

This is why environmental factors can affect someone's propensity towards addiction, if you increase their stress levels enough, they will look for any way to relieve that stress and will be compelled to continue to do so.

Socioeconomic factors

In the modern day socioeconomic factors are the main stressors that could cause the chronic inescapable stress. One particular study in Yazd[32], Iran, performed an opinion survey, in which they interviewed the spouses of male addicts and asked them to rate different socio-economic factors on their effectiveness on causing their spouses addiction. They were asked to rate the factor from 1 to 5, 1 being the least effective and 5 being the most effective. The results of this study concluded that multiple risk factors had a statistically significant effect on risk of addiction, and are collated below.

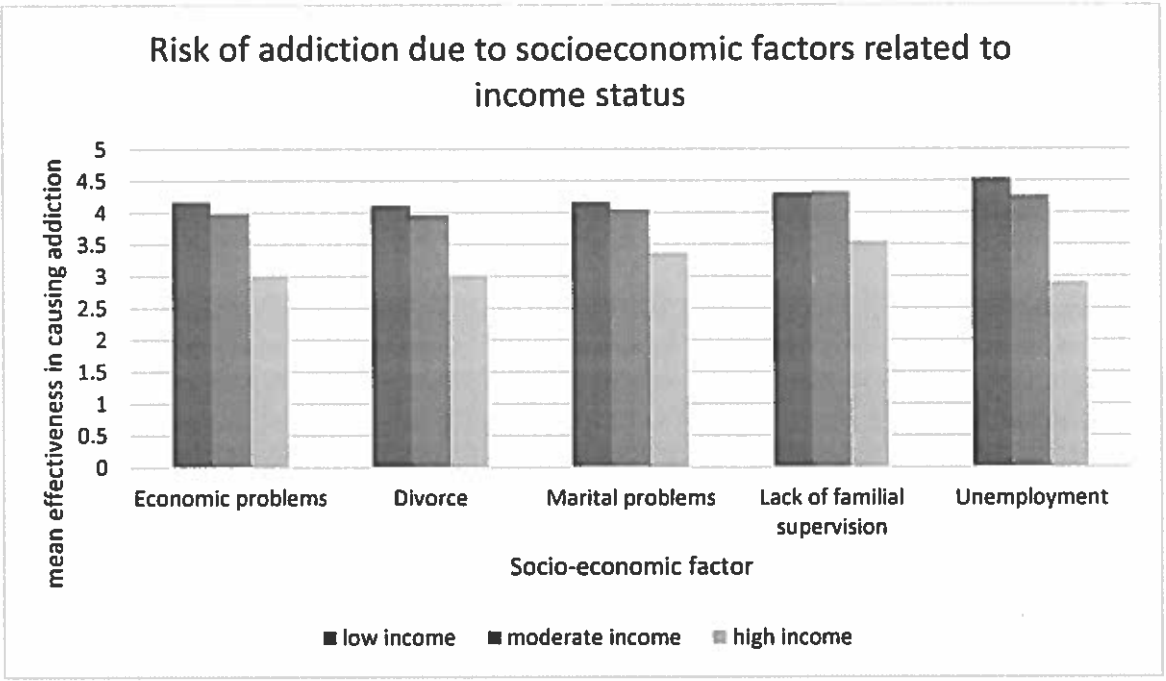
[30] (Sinha, 2001)
[31] (Ronald A Ruden, 2001)
[32] (Zahra Pourmovahed, 2013)



As stated in the methodology of this study, these are opinions and are subjective, meaning there is reason to treat the data with a certain level of scepticism. However, with a sample size of 261 spouses, it is more reliable as a large amount of people appear to be in agreement that these are important factors.

These socioeconomic factors would cause a propensity towards addiction in many ways. Ease of availability, friends who are addicts and addicts in the family would lead to an opinion of drug abuse and addiction being more normal and acceptable, thus lowering social barriers that may in other communities deter individuals from drug use. Unemployment, marital problems/divorce and economic problems are likely causes of chronic inescapable stress which could drive people towards the use of substances as part of a coping mechanism that leads into a coping mechanism. lack of familial supervision and lack of recreational facilities removes the opportunity for healthy coping mechanisms to take place and could force individuals towards more damaging coping mechanisms in the form of drug abuse.

Another interesting observation of this study is that the mean effectiveness rating, of certain factors, given by the spouse was affected by the economic status of the family. The results showed, on average, a decrease in the effectiveness of certain factors with an increase in income of the household, as demonstrated below.



As shown by the graph there is a clear decrease in the mean rating given to each factor with the increase in income status. This lends credibility to the idea that those who are in areas of poverty are at a higher risk of becoming addicted. However, I would speculate that it is not just the income status that causes the increased risk, but the conditions associated with the income status. For example, impoverished areas have been shown, by some studies, to have higher crime rates, and will therefore encourage the normalisation of illicit activities, including illicit drugs.

Another study[33] shows a similar trend in that whilst prevalence of alcohol abuse increases with an increase in income, there is an increase in the number of cases of alcohol dependence as income decreases. Thus, lending credibility to the idea that low income has a knock-on effect on other socioeconomic factors which increases the propensity towards addiction.

However, I doubt in any case that these factors act in isolation, as a person's life is dynamic and so damage or alteration in certain areas of their life will no doubt have severe impacts on other areas of their life. For example, divorce could cause a lack of familial supervision on the children and perhaps also some deal of stress and upset causing them to seek some form of outlet, and suppose that there is a lack of recreational facilities and easy availability of drugs. There are examples of such situations that show the intervention by use of healthy outlets can decrease the probability of people lashing out[34]. This suggests that the correct environmental setup could limit someone in dire circumstances to few other alternatives than lashing out in an unhealthy manner, as demonstrated by the above study.

Some of these factors may also perpetuate addiction within a person or across generations. For example, living in an area where addiction is common and there is easy access to drugs, it would be extremely difficult to break the addictive cycle, as any memory associated with the use of drugs acts as a cue to a recovering addict, which then triggers a craving. Therefore, for a recovering addict,

[33] (Keyes, 2008)
[34] (Gärtner, 2008)

being surrounded by cues such as addicts, dealers and people using drugs would trigger constant craving and most likely relapse. Also certain factors could perpetuate the addiction across a generation, for example living with an addict could normalise the abuse of substances or addictive behaviour, and if they acted as a role model, the next generation could be heavily influenced by their behaviour. Therefore, leading the cycle of addiction to be continued within one generation or across many. I believe that having addicts in the family, friends, or generally role models, who are addicts is a very prevalent factor in causing a propensity towards addiction because of its ability to, in effect, create a lineage of addicts.

This study is not stand alone in its findings; there are studies that have also observed such results with factors such as unemployment[35], lack of supervision[36] and drug availability[37] as pertinent factors in causing a propensity towards addiction.

Conclusion

From the research I have done and the critical evaluation of each factor considered I am led to conclude that whilst genetic factors do play a significant role in the process of addiction they are not the most important factor to consider in the propensity of an individual towards addiction.

The reason I have decided this is because as far as I can see the only way for someone to become addicted is for them to first be in a scenario in which addiction is an option. For example they would need sufficient reason to turn to addictive behaviour, some form of chronic stress in their life that they feel the need to escape from. They would need to then have a lack of healthy outlets to relieve this stress through to cause them to turn to other sources and they would also need to be in an area where either the addictive substance or activity was available for use. Only then would they come into contact with the addictive substance or activity, and only then would the genes have a major role to play in the process. However, between the stress and then becoming addicted there are so many different failsafe's in the environmental conditions such as those listed above in the socio-economic factors section which could provide potential barriers to stop the person ever coming into contact with the addictive substance or behaviour. Environmental factors are the first line of defence against addiction and with the correct environmental conditions it could be possible for someone with the highest genetic propensity towards addiction to never come across addictive substances or behaviour.

However, I do believe that the genetics behind addiction play an important role in a person's propensity towards addiction, only that this role takes place at a later state, once the person has begun the addictive cycle and first tried the substance or behaviour. It is at this point that I believe genetics is nearly the sole factor that dictates how easily the self-perpetuating, spiralling condition of addiction begins. So in a way I do conclude genetics play a large role in propensity towards addiction, just only once other environmental factors have first been fulfilled.

A well written piece with fluid communication of findings and a logical argument synthesised into thought. AO3 Co/R

[35] (unknown, 2014)*
[36] (UNDOC, unknown)
[37] (ME Barrett, 1990)

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Evaluation of sources

In this section I will be critically analysing the reliability of the sources I have used in my project.

One of the key sources of information in this project was PMC or Pubmed, a collation of medical studies by the US national library of medicine and national institutes of health. These are government run organisations and so can be considered as reliable sources of information. This, along with the fact that all of the studies I have used from this library have been individually performed by either universities or recognised institutes, allows me to consider them as reliable sources as these organisations are acting in the pursuit of information and shouldn't be influenced by ulterior motives.

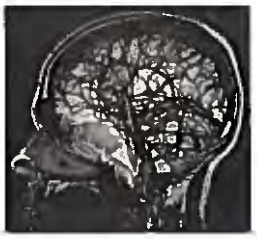
I have used certain websites to increase my understanding of the brain structures and their functions, such as mentalhelp.net, neuroscientificallychallenged.com and serendip.com. However, I have always ensured that the information I found was in concordance with that found in other sources including the 3D brain app, which I consider a trustworthy tool as it was created for educational purposes.

I have upon one occasion referenced Wikipedia as a source, however, I investigated numerous cited sources of information within the section I used and they appeared to be of scientific origin and not made up. I further checked this information using quick google searches and found multiple other publications to be in agreement with the information, however I have cited Wikipedia as it is the best collation of necessary information I could find.

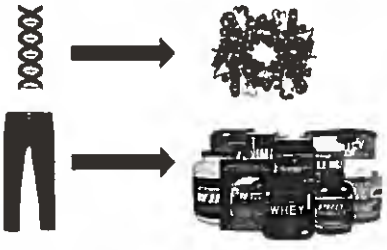
I have used some sources which I consider questionable, in that I do not know their motive and can't be sure of the quality of information there, in these cases I have further researched the topic and found other sources of similar quality in concordance with the information. Whilst this increases the reliability of the information somewhat, I have still marked all sources considered questionable with an asterisk in the footnotes.

I have upon one occasion listed UNDOC as a source, in which it details addiction treatment and how supervision is a key element of treatment. I have extrapolated this information to the idea of a preventative measure, by the logic that if supervision can help addicts recover it could also prevent addiction from initially occurring.

ADDICTION AND GENETICS



WHAT ARE GENES?



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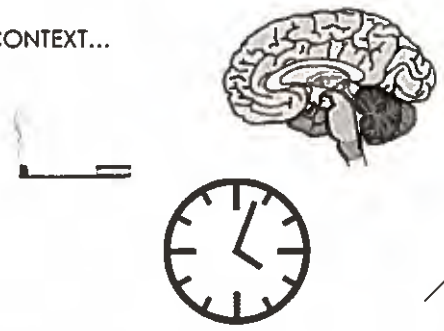


ENVIRONMENTAL FACTORS

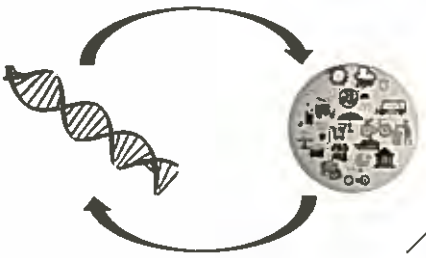

CONCLUSION

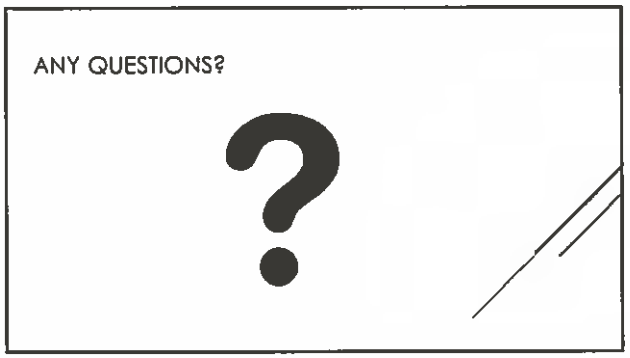
METHODOLOGY



PubMed


EVALUATION





AO4 Lv III a well structured + engaging presentation that showed impressive knowledge on the subject as well as his calm, authoritative presentation style and his ability to reflect critically and analytically on the whole process.