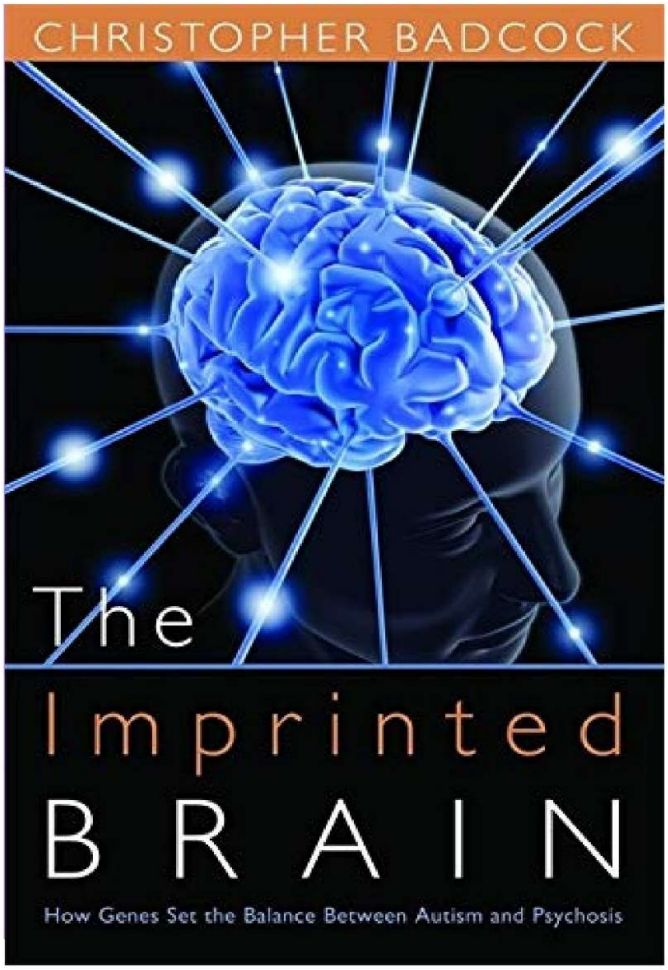
The imprinted brain

An interdisciplinary and international bachelor course offered by Utrecht University and the University of Leeds



Inspired by Christopher Badcock's book *The imprinted brain.*

February – April 2021

Colofon

As a collaboration between Utrecht University (the Netherlands) and the University of Leeds (UK), a Collaborative Online International Learning (COIL)-based bachelor course called 'The imprinted brain' has been designed, developed and implemented. This international and interdisciplinary online course deals with the molecular genetics of autism and psychosis spectrum disorders. The course is run simultaneously at Utrecht University and the University of Leeds, with students with different disciplinary backgrounds from both universities, and with teachers from both universities.

A Moodle®-based learning platform is used in this course. The following pages describe the full content of the learning units (LUs) on this electronic learning platform, as offered during the 2021 course. For a menu-like overview of the LUs on the platform, please see appendix 1a.

A warm welcome

Welcome to the module 'The imprinted brain'!

Allow us to introduce ourselves.

My name is Liesbeth Bijlsma. I am one of the teachers of this course, and was involved in the development of it. I am an assistant professor specialized in psychopharmacology, i.e. the effects of drugs on the brain and behavior. My main interest is how emotions are regulated in the brain and what changes in neuronal signaling are involved in mood disorders. My current research focuses on the role of serotonin in anxiety. I'm really looking forward to work with you in this course, because I am fascinated by how the brain regulates behavior and I believe developing a broader, interdisciplinary perspective on this will really help to get a better understanding of, and provide more effective solutions for, important societal and medical questions related to psychiatric disease.

My name is Ferdi Engels. I am the coordinator and one of the teachers of this course and also was involved with the development of it. I am a pharmacologist by training. My main expertise lies in receptor pharmacology and pharmacodynamics (i.e. quantitative receptor pharmacology). I have been fascinated by the brain for a long time, however. This is why I am very thrilled to work together with you in this course.

My name is Ian Wood. I am one of the teachers of this course from the University of Leeds. I am a Biochemist by training and I have focused on gene regulation and epigenetics in the nervous system through my research career since my first degree. I have been fascinated by how changes in gene expression affect our behaviour and contribute to diseases of the brain. My current research focuses on the role of epigenetics and microglia in the development of Alzheimer's disease. This course brings together a number of areas that I am interested in and I am looking forward to working with everyone on it.

My name is Hugh Pearson. I am one of the teachers of this course from the University of Leeds and Programme Leader for the Neuroscience degree. I am interested in ion channels and neurodegeneration and use electrophysiology to measure specific ion channel activity in neurones and their response to beta amyloid in Alzheimer's disease.

Before you start

There are a few things that you need to know before you start the module. You will find them in these introductory learning units. We recommend you to finish this part before the module starts.

Learning Units

This e-learning module is made up of different *learning units* (LU) that you need to complete. Each learning unit ends with the button labeled 'complete'. Please click on the ‘complete’ button each time you have completed a learning unit. At some activities, this button will not be visible to you. This means that you

will have to – for example - submit an assignment or post a discussion topic to complete this learning unit.
Learning units marked by a red * are required components.

Progress

You will always be able to go back to learning units that you have already finished. On the upper right of your screen you will see your progress. Your progress is based on the activities that you have completed. Next time you go to this online platform, the first learning unit that has not been completed will be on top of your screen.

If you have any questions about the learning environment, you might find the answers at the FAQ at the top of each page. The FAQ is in Dutch, but an English translation is offered through a link at the top of the page. If you cannot find the answer at the FAQ, you can ask your questions about this learning environment down below (by posting a remark).

A word about words

In 'The imprinted brain' we work and learn together, as students and teachers with different backgrounds and from different countries. One of the instruments that we use to work together is language. For practical reasons we will use the English language. However, there are different varieties of English language (British, American, Canadian, Dutch?). Let's help each other understand each other.

Two words need some explanation right away: course and module.
'The imprinted brain' is called a **course** in Utrecht, but is called a **module** in Leeds. In Leeds a course, e.g. Neuroscience, will lead to a bachelor degree and is composed of several modules. In Utrecht we would call this an 'opleiding'. Curious how to pronounce this? Ask your Dutch fellow student.

Let's agree to call 'The imprinted brain' a module.

About this module

The module is about the possible role of epigenetics in the development of autism spectrum disorders and psychosis. Central to the module is a thought-provoking book by Christopher Badcock, "The imprinted brain" (2009). It describes a radical new theory of the mind and mental illness based on the discovery of genomic imprinting. Imprinted genes are those from one parent that, in that parent's interest, are expressed in an offspring rather than the diametrically opposed genes from the other parent. For example, a higher birth weight may represent the dominance of the father's genes in leading to a healthy child, whereas a lower birth weight is beneficial to the mother's immediate wellbeing, and the imprint of the mother's genes will result in a smaller baby. According to Badcock's view, a slight bias for the father's genes may result in autism, whereas bias for the mother's genes may result in psychosis. A state of equilibrium - normality - is the most likely outcome, with a no-win situation of balanced expression. Imprinted genes typically produce symptoms that are opposites of each other, and Badcock uses psychiatric case material to show how many of the symptoms of psychosis can be shown to be the mental mirror-images of those of autism.

Module objectives

Upon completion of this module, you will have knowledge and comprehension of the role of epigenetics in health and disease. Specifically, you should:

- understand the concept of epigenetics, its molecular biology and its role in normal physiology and in pathophysiology
- understand the pathophysiology, symptoms, and treatment options of autism spectrum disorders and of psychosis
- be able to defend or dispute Badcock's theory of the Imprinted Brain
- be able to collaborate with students with a different academic background (neuroscience, pharmacy, biology, chemistry, medicine, dentistry, etc.) and different nationalities and cultures (e.g. Dutch, British)
- be able to engage in interdisciplinary learning and possess the skills to work in interdisciplinary teams

Module design

To meet the module objectives, collaborative learning will be used. You will be working in small study groups with students from different disciplinary backgrounds. The module design will allow you to work together during online meetings (synchronous learning activities) and outside of these meetings (asynchronous learning activities).
Collaborative learning can take shape in many ways. We will be using so-called Reciprocal Peer Tutoring (RPT). You don't know what this is? We will explain in

the introductory meeting. But, you might as well try to find out yourself by Googling it....

Assessment

A special word about assessment? Why?

It is known that assessment plays a very powerful role in students' learning. All learning activities should be in line with both the module objectives and the assessment. It is therefore important that you know what we expect from you, and what you can expect in this module.

In this module the assessment consists of:

Formative assessment, feedback on learning, self assessment.

Several learning units offer activities (quizzes, assignments, group discussions etc.) to test your knowledge. Also, online class meetings may offer ways of checking how you are doing.

Summative assessment, being part of the final grade.

For students from the University of Leeds (UoL), the final grade is composed of:

1. An individual exam (100%) dealing with the topics of the learning units presented in weeks 1 - 7.
2. Deliverables, collected in an individual portfolio (pass/fail).

For students from Utrecht University (UU), the final grade is composed of:

1. An individual exam (70%) dealing with the topics of the learning units presented in weeks 1 - 7.
2. A group project report (30%) about the longitudinal interdisciplinary project.
3. Deliverables, collected in an individual portfolio (pass/fail).

Introduce yourself

Think of a room full of newly-arrived strangers – not yet a group, but a collection of individuals. At the meeting and greeting stage you introduce yourself, say a little about yourself and listen and respond to others as they introduce themselves. It is all part of the warming up process. In the virtual room that you are entering when you attend the introductory meeting, it's much the same – only you can only see your fellow participants on screen.

Assignment

In this assignment you will introduce yourself to your fellow students. By doing so, your fellow students get to know you, even if they do not meet you in person.
Please prepare a 1-slide PowerPoint presentation in which you introduce yourself. During the introductory meeting you will get 1 - 2 minutes to tell something about yourself using your PowerPoint presentation. Your slide must at least contain a photo/selfie of you and your name. It is up to you to fill your slide and your 1 - 2 minutes to reveal who you are and what makes you tick.

First meeting on Monday February 8, 2021, online in MS Teams

This is the first online meeting of the module 'The imprinted brain'.
We will have time to:

- Get to know each other a little bit
- Share information about the module
- Ask and answer questions
- Get into the mood of learning about the imprinted brain

Week 1 About ASD and PSD

LU 1.1 Introduction

Introduction

Autism and psychosis seem totally unrelated disorders. In psychology textbooks these disorders are described in different categories: autism is considered a developmental disorder, whereas psychosis represents a symptom associated with mental disorders like schizophrenia. Nevertheless, researchers Christopher Badcock and Bernard Crespi have put forward a theory* which states that autism and psychosis represent extremes of a continuum of behavioural traits, making these disorders diametrically opposed to each other.

During the first three weeks of this module you will study the pathophysiology and symptoms of autism spectrum disorders (ASD) and psychosis spectrum disorders (PSD) from a psychological perspective and you will get insight in the role of the social brain in both spectra of disorders.

* *Crespi B, Badcock C (2008) Psychosis and autism as diametrical disorders of the social brain. Behavioral and Brain Sciences 31: 241-320*

Learning outcomes

Learning activities within the psychology theme contribute to the following general learning outcomes:

- Describe the pathophysiology, symptoms, and treatment options of autism spectrum disorders.
- Describe the pathophysiology, symptoms, and treatment options of psychosis spectrum disorders
- Describe the concept 'the social brain' from a psychological and neurobiological perspective.
- Critically evaluate the imprinted brain theory with the use of arguments from different disciplinary perspectives.

Resources

Crespi Badcock 2008 - review imprinted brain theory.pdf

LU 1.2 Self-study assignment 1A - Autism spectrum disorder

SELF-STUDY 1A: AUTISM SPECTRUM DISORDER

Introduction

In many textbooks and information leaflets, autism is said to be a developmental disorder characterized by difficulties with social interaction and communication, and by restricted and repetitive behavior. Sounds heavy, doesn't it? Let's first start, however, with an open mind and assume that autistic people are just different.

Specific learning outcomes:

After this self-study you are able to:

- describe the major characteristics of autism spectrum disorder and the levels of severity used to accommodate the range of difficulties experienced.
- describe the current ideas about possible biological and psychosocial causes of autism spectrum disorder.
- name the main treatment options for autism spectrum disorder currently available.

Literature:

- Barlow – Abnormal Psychology an integrative approach, 8th edition (2018). Chapter 14.
- DSM-V (for reference)

Assignment 1:

Watch this animated explanation of autism (5:30 min).

https://youtu.be/6fy7gUIp8Ms

We know that there is not one autism but many subtypes. Because autism is a spectrum disorder (a range of linked conditions, sometimes also extending to include singular symptoms and traits), each person with autism has a distinct set of strengths and challenges. The ways in which people with autism learn, think

and solve problems can range from highly skilled to severely challenged. Some people with autism may require significant support in their daily lives, while others may need less support and, in some cases, even live entirely independently. This will also be clearly shown in Louis Theroux's documentary on autism which you will watch in preparation of Thursday's meeting.

Everybody with autism is different...

... but there are general signs and symptoms that are associated with autism.

Assignment 2:

Use chapter 14 from Barlow's Abnormal Psychology to answer the questions below. Construct a table with a column labeled 'autism', containing your answers from this learning unit. In the next learning unit (LU 1.3) you will expand the table with a column labeled 'psychosis', so that you can compare these disorders. The information gathered in this self-study assignment will be used during **meeting 2**

QUESTIONS

Try and answer the following questions to get more insight in autism:

1. What is autism?
2. What are signs and symptoms associated with autism?
3. What separate conditions fall under the range of autism spectrum disorders (ASD)?
4. What might cause ASD?
5. How does screening and diagnosis of ASD take place?
6. What treatments are available for ASD?

Resources

Barlows Abnormal psychology - chapter 18 Autism.pdf
DSM-V Autism.pdf

LU 1.3 Self-study assignment 1B - Psychotic spectrum disorder

SELF-STUDY 1B: PSYCHOTIC SPECTRUM DISORDER

Introduction

Psychotic spectrum disorders are a family of disorders in which psychosis, a loss of contact with reality, is the most important hallmark. Schizophrenia is the best-known member of this spectrum of disorders. Schizophrenia is a severe psychiatric disorder, often associated with considerable impairment of daily life of both patients and their families.

Specific learning outcomes:

After this self-study you are able to:

- describe the main symptoms of schizophrenia.
- name four different types of psychotic disorders and state at least one way in which each is different from schizophrenia.
- discuss pathophysiology of schizophrenia, including genetic and neurodevelopmental factors and structural and functional brain abnormalities.
- describe the different treatment options for schizophrenia.

Literature:

- Hooley – Abnormal Psychology 17th edition (2017). Chapter 13.
- DSM-V (for reference)

Assignment 1:

"I don't have psychosis, but I have a psycho sis", someone joked. What is psychosis? Watch this (2:59 min).

https://youtu.be/RRGGxK3OpNc

Psychosis has a large impact on the sufferers and their friends and family. It is sometimes so difficult to understand. Check out Simon's story (4:59 min).

https://youtu.be/GUEb7hPHf3M

Assignment 2:

Use chapter 13 from Hooley's abnormal psychology to answer the questions below. Include your answers in the table that you constructed in LU 1.2. Observe similarities and differences. The information gathered in this self-study assignment will be used during **meeting 2.**

Try and answer the following questions to get more insight in psychosis:

1. What is psychosis?
2. What are signs and symptoms associated with psychosis?
3. What mental disorders are characterized by psychotic symptoms?
4. What might cause psychosis spectrum disorders (PSD)?
5. How does screening and diagnosis of PSD take place?
6. What treatments are available for PSD?

Resources

DSM-V psychosis.pdf
Hooleys abnormal psychology Chapter 13 psychosis.pdf

LU 1.4 Self-study assignment 2 - Daily life with ASD and PSD

Self-study 2: DAILY LIFE WITH PSD AND ASD

Watch the two documentaries presented below. Keep the questions from self-studies 1A and 1B in the back of your mind and make notes of interesting scenes that relate to the symptoms and characteristics of ASD and PSD. You will work with this information during **meeting 2.**

- “Extreme love”, about autism (Louis Theroux, BBC TWO)
- “Why did I go mad”, about psychosis (Horizon, BBC TWO)

you can find the documentaries **here**

LU 1.5 Meeting 2 - Clinical practice and daily life with ASD and PSD

Introduction

Most textbooks on abnormal psychology include short descriptions of actual clinical cases. However, those presentations are necessarily brief and too fragmented for students to gain a clear understanding of the unique complexities of a person's troubled life. The documentaries you watched as preparation do provide a richer experience of the lives of people with ASD and PSD.

Specific learning outcomes:

- After this meeting you will be able to give concrete examples of daily life experiences and situations related to the symptoms of ASD and PSD as formally described in the DSM-V criteria.

Literature:

- Barlow – Abnormal Psychology an integrative approach, 8th edition (2018). Chapter 14.
- Hooley – Abnormal Psychology 17th edition (2017). Chapter 13.
- DSM-V (for reference)

Instruction
During this meeting you will work in small groups (7 students) in your own MS teams group channel. Each group will be assigned either PSD or ASD. Start a videomeeting in your group channel and work on the assignments below. If you have questions, you can ask the teacher to join your videomeeting, by calling him/her using the *@name teacher* function in the chat. The teacher will also pro-actively join at some point during the group discussion to ask how you are doing.

Assignments:

- Discuss the documentary related to the assigned disease and try to link the symptoms described in the assigned book chapter to relevant examples from the documentaries.
- Select some scenes that you can use to illustrate the symptoms, you can make screenshots for later reference.

- Draw a concept map in which you visualize the links between the symptoms and the examples from the documentaries (also include timeframe from relevant scenes).
- Compare treatment policies from United Kingdom and the Netherlands for the assigned disease.
- Useful resources are the National Institute for Health and Care excellence (NICE) website for UK (www.nice.org.uk) and the "*Akwa GGZ kwaliteitsstandaarden*" for NL (www.ggzstandaarden.nl).

During the last 30 minutes of the session, some of you will be asked to share their insights. After the meeting, all concept maps will be shared via MS Teams.

NB Also add the conceptmap you created as a group to your personal portfolio. For now, you can just set up a portfolio folder in your personal documents. Lateron we will clarify how you can hand in your full portfolio at the end of the module.

Week 2 The social brain

LU P2.1 Introduction interdisciplinary project

Introduction

This project is part of the module 'the imprinted brain' (FA-BA219) and its main outcome is an up-to-date literature review that discusses a self-formulated problem in relation to the prevention or treatment of autism spectrum disorder or psychotic spectrum disorder from an **interdisciplinary perspective**. During this project you will collaborate with three other UU- students (project groups consisting of four students) from different disciplines. You will work together on the same research question but each of you will take another perspective (discipline). In the final stage of the project, you will integrate all the different perspective in order to formulate an overarching, integrated answer to your research question.

Learning outcomes

Upon completion of this project, you will be able to:

- Select disciplines that are relevant for answering a specific research question.
- Describe the current views on ASD and/or PSD from a variety of disciplines relevant for a specific research question.
- Communicate with peers from different disciplines within the context of the module theme.
- Collaborate with peers from different disciplines on a literature study in order to answer a specific research question.
- Critically evaluate literature from different disciplines relevant for a specific research question, discuss common ground between these disciplines and formulate an integrated answer for this research question.
- reflect on using an interdisciplinary approach and its added value for understanding ASD and PSD and answering the specific research question.

Assessment of project

- The end product of the project will be a written report and a short pitch during an online symposium in week 10

Overview of the project

For detailed explanation of different phases presented in the overview, see LU P2.2

Phases	Learning activity
Preparation	**LU P2.1** Introduction interdisciplinary project **LU P2.2** Background information interdisciplinary research **Meeting February 16th:** **LU P2.3** Team up! **LU P2.4** Defining your research question **LU P2.5** Peer feedback on research question
1. Disciplinary grounding: • Searching and extracting disciplinary-relevant information • Analysing and summarising disciplinary information	**LU P3.1** Consultation meeting February 23rd - research question **LU P3.2** Literature survey - Searching relevant literature - Data Management **LU P5.1** Consultation meeting March 9th - literature research **LU P6.1** Consultation meeting March 16th - literature research **LU P8.1** Disciplinary grounding: Discussing disciplinary findings from different perspectives (meeting April 1st)
2. Perspective taking – discovering common ground: • Finding connections between disciplines • Combining disciplinary knowledge to identify interconnections	**LU P9.1 Perspective taking & common ground**: Identify differences, connection, and overlap between insights (Meeting April 6th)
3. Integration Gaining new insights, creating new products, …. in ways that would have been impossible through single disciplinary means.	**LU P9.2 Integration**: Formulate integrated conclusions (Meeting April 8th) **LU P10.1** Pitches project (meeting April 15th) **LU P10.2** Finalize project paper

Resources

For the project, we will regularly refer to the following book

An Introduction to Interdisciplinary Research : Theory and Practice, edited by Steph Menken, and Machiel Keestra, Amsterdam University Press, 2016. ProQuest Ebook Central.

The book is freely available for UU students via the link below.

Resources

https://ebookcentral.proquest.com/lib/uunl/detail.action?docID=4460743

LU P2.2 Background information interdisciplinary research

Interdisciplinary research

In this module we will use the following definition of interdisciplinary research: *Interdisciplinary research is research in which relevant concepts, theories and/or methodologies as well as the results or insights these disciplines generate, are integrated.*[1]

The approach of interdisciplinary research is to study a complex topic or problem whose parts are the focus of two or more disciplines, integrate their insights, and construct a more comprehensive understanding of the topic or problem.

The table below shows the differences between disciplinary and interdisciplinary approaches to research.

Table 10.1 Comparison of Disciplinary and Interdisciplinary Approaches to Research

Disciplinary Approach	Interdisciplinary Approach
1. The problem in its entirety must fall within the discipline's research domain to be considered researchable by the discipline.	1. The problem must be complex (i.e., have parts requiring insights from two or more disciplines).
2. Limited to a single disciplinary perspective	2. Inclusive of all relevant disciplinary perspectives
3. Uses the discipline's favored method	3. Uses an overarching process
4. Does not critically analyze insights from other disciplines	4. Critically analyzes insights from relevant disciplines
5. Does not integrate insights from other disciplines	5. Integrates insights from relevant disciplines
6. Product of research is an understanding or conclusion that is limited to the contributions of a single discipline	6. Product of process is an understanding that is more comprehensive than the contribution of any single discipline

Table 1: from Repko A.F., Szostak R., Buchberger M.P. (2017) Introduction to interdisciplinary studies, 2nd ed.

Interdisciplinary research question

During this project, you will formulate a research question within the scope of the imprinted brain. This research question must meet certain conditions.

Criteria for the research question[1]:

- researchable, doable in time and scope
- open-ended (not a yes/no question)
- well-formulated, in every-day language
- disciplinary neutral
- no disciplinary jargon
- no personal bias

Steps in interdisciplinary research

For this project we will use a step-by-step approach, specifically designed to study complex problems from an interdisciplinary perspective.

These steps are:

1. **Disciplinary Grounding**
   Disciplinary grounding involves having a basic knowledge and understanding of the different disciplines involved in your research question, as well as ways in which their knowledge is constructed, validated and communicated.
2. **Perspective taking and discovering common ground**
   Perspective taking involves analysing the problem from the standpoint of each interested discipline and identifying their commonalities and differences. It also encompasses an attitude of open mindedness to- and valuing of different perspectives, and the willingness to reflect on of one's own biases and assumptions.
   Common ground is the shared basis between (conflicting) disciplinary insights or theories. Finding common ground also includes identifying overlap/commonalities between disciplines. This is a creative process that involves modifying or reinterpreting disciplinary elements that conflict. Assumptions from two or more disciplines are made explicit and are compared, and some degree of overlap between disciplinary perspectives are identified. It also incorporates the identification of how terms are used differently in different disciplines and defining problems explicitly in neutral terms that and creates a common vocabulary that can be applied to the object of study.

3. **Integration – better understanding, new insights**
   Integrating perspectives involves gaining new insights, creating new products, …. in ways that would have been impossible through single disciplinary means. Integrating perspectives is a creative process, and can take many forms, such as developing a new model, a metaphor, a method, or a future scenario. Integrating also encompasses having confidence and intellectual courage (out-of-the-box thinking).

Preparation for the first project meeting on February 16th:

Read pag. 25-33 from *An Introduction to Interdisciplinary Research: Theory and Practice* (Chapter 3 -5)

---

[1] Menken & Keestra, *An introduction of interdisciplinary research, theory and practice* (2016).

Resources

https://ebookcentral.proquest.com/lib/uunl/detail.action?docID=4460743

LU P2.3 Team up!

Team up! – meeting February 16th, 13:15-14:00 hrs

1.1 Introduction to different disciplines

During this project you will work together with students from different disciplines. The first hour of this meeting we will spend on getting to know your fellow students better and learn more about their disciplines.

For this assignment you will work in your MS Teams project-group channel

You probably already discussed during week 1, but before you start with this assignment, make sure everyone is aware of your disciplinary background.

Think: After all students told their name and discipline, write down (**for yourself**) what you think the discipline of the other person has as a main interest (e.g. what would someone from department Pharmacy, Biology, Medicine, Psychology, do? What would they focus on in their study?

Pair: Discuss your ideas with one of your fellow students: is this correct?

Share: Share your findings within your project group

1.2 Teamwork

Introduction

Learning to cooperate in teams starts with being aware of your own strengths and weaknesses. Below you find a list of teamwork skills. You are asked to indicate how satisfied you are with your own skills, and to answer the reflection questions.

Teamwork skills

Learning to cooperate in teams starts with being aware of your own strengths and weaknesses. Below you'll find a list of teamwork skills. You are asked to indicate how satisfied you are with your own skills, and to answer the reflection questions.

Teamwork skills	*Not satisfied*	*Little satisfied*	*Very satisfied*
1 Reliable and committed (taking responsibility and being accountable)	◯	◯	◯
2 Communicative (explaining your thoughts clearly)	◯	◯	◯
3 Active listening (listening carefully and ask questions to clarify others' ideas)	◯	◯	◯
4 Participate actively (being prepared and contribute constructively)	◯	◯	◯
5 Sharing your ideas (readiness to share your knowledge and feelings with the team)	◯	◯	◯
6 Flexible (Compromising when necessary to move the group forward)	◯	◯	◯
7 Creative problem solving (being able to come up with solutions and new perspectives)	◯	◯	◯
8 Conflict resolution (being able to mediate problems between team members, focusing on solutions rather than blaming others)	◯	◯	◯
9 Respectful (conveying respect for others and for their ideas)	◯	◯	◯

Reflection on your teamwork skills:

1 I am proud of my ability to: ……..

2 I intend to improve my ability to: ……

Please share your reflections with your group and try to find out what your strengths are as a team, and how you could cope with the weak spots of your team.

Finally make a summary of your group weaknesses and strengths and put it the files section of your project-groupchannel. Save your personal reflection for reference, as you will need this for your reflection assignment at the end of the module.

When finished, continue with the second part of this meeting. You can find instructions in LU P2.4

Resources

Teamwork skills.docx

LU P2.4 Defining the research question

Meeting February 16th, 14:15-15:00

Defining the research question

The research questions for the interdisciplinary research projects should be within the scope of the following two objectives:

1. **Can we prevent the development of autism spectrum disorders (ASD) and psychotic spectrum disorders (PSD)?**

   (possible disciplinary angles: epidemiology, biology of disease, neurology, pathophysiology, pedagogy/upbringing, psychology, sociology? (societal change that some individuals have more problems adapting to than others), molecular genetics, ethics, lifestyle etc.)

2. **Can, and should we, treat patients with autism and psychotic spectrum disorders?**

   (possible disciplinary angles: epidemiology, biology of disease, neurology, pathophysiology, psychology, sociology, molecular genetics, health economics, ethics, pharmacology, psychiatry, surgery, etc.)

ASSIGNMENT 1: Brainstorm

Brainstorm within your project group about ideas that would be interesting to research within the scope of above mentioned objectives.

Everything is possible, there are no boundaries, and –very important- only positive feedback is allowed during the brainstorm session. No “yes, but…” in this stage. All ideas are written down.

Make notes of all the different ideas that come up.

ASSIGNMENT 2: Defining the research question

a) In this stage, the best ideas are undergoing a reality test, based on four criteria:

1. The topic fits within the scope of the module.
2. The topic is *interesting* to all four of you.
3. The topic is *complex*; impossible to solve from the perspective of just one discipline/approach.

4. The topic should be *relevant*; this means explaining why we should care about the answer to the question.

b) Choose one topic to pursue.

c) Specify your idea and redefine it in the form of a (concept) research question.

Criteria for the research question (Menken & Keestra)

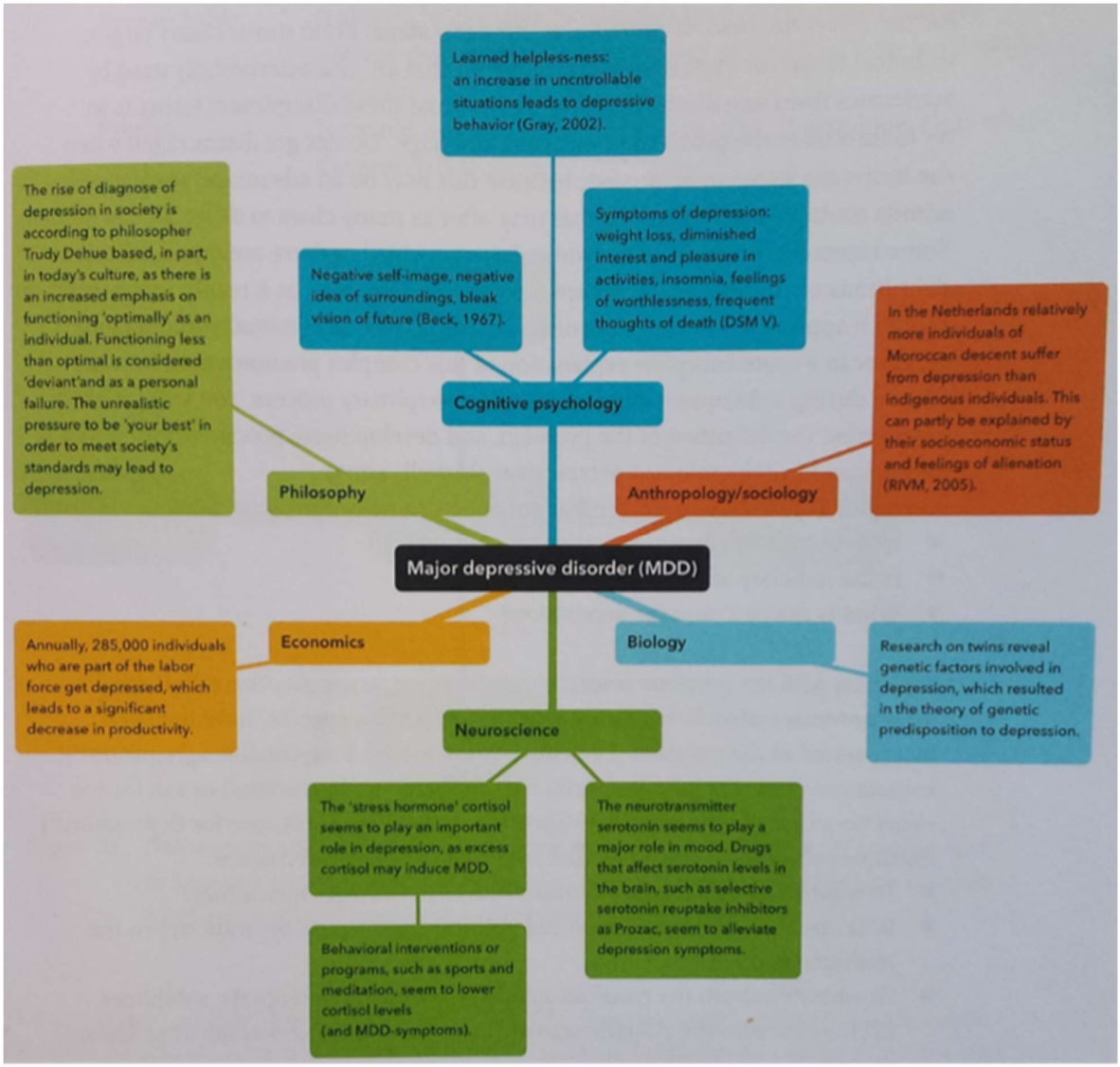
- researchable, doable in time and scope
- open-ended (not a yes/no question)
- well-formulated, in every-day language
- disciplinary neutral
- no disciplinary jargon
- no personal bias

d) Try to identify which disciplinary insights are relevant to the problem.

e) Select the most relevant 4 disciplines.

In selecting disciplines, you could choose the most dominant insights, or those that are covered in your team. A mind map or concept-map may help you to get an overview of the most relevant main disciplinary theoretical perspectives. In the example below, six disciplinary perspectives to major depressive disorders are presented.

f) Once you have decided which disciplines are most relevant to include in your research, it is useful to define sub-questions for each of the chosen disciplines. (see - below for example from: Interdisciplinary Research, Keestra & Menken, ISS -UvA, pag. 65). Start with what you already know about this topic from your own discipline.



ASSIGNMENT 3 Elaboration and summary

After the meeting, continu collaboration within your group and write a one-page summary about your topic including the specific research question you would like to address, the multidisciplinary nature of the specific research question and a short overview of what you already know about this topic.

Upload the summary with your research question and sub questions to the files section of the MS teams "TIB 2021 project' environment (folder 'research questions') before **Thursday February 18th noon**. Explicitly include your group number in the file name!
You will receive feedback on your summary and research question from two other project groups and your project supervisor.

LU P2.5 Peer feedback summary & research question

Instruction peer feedback summary & research question

Give feedback to at least two other groups, the scheme below shows which two groups you definitely have to give feedback on. Deadline for feedback is **Monday February 22nd, noon**.

group	**gives feedback on:**	
1	2 and	3
2	3 and	4
3	4 and	5
4	5 and	6
5	6 and	7
6	7 and	1
7	1 and	2

Read the summaries of the other groups and **write** feedback using the following questions for your feedback:

1. Introduces the topic or problem that is the subject of the study and states the purpose or objective of the study.
1.1 The authors define the problem or topic in a way that is appropriate to interdisciplinary study.
1.2 The authors clearly define the scope of the study.
1.3 The authors avoid the three tendencies that run counter to interdisciplinary process: disciplinary bias, jargon, and personal bias.
1.4 The authors explain the relevance of the question.
2. Explain why the problem or topic requires using an interdisciplinary approach.
2.1 The authors state that the problem or topic is complex and explains what this means.
2.2 The authors states or imply that there are important insights in the problem or topic offered by two or more disciplines.
2.3 Explains the relevance of each discipline for the problem or topic.

Upload your feedback to the MS teams files section, folder 'research question'. Explicitly add 'feedback group X on group Y' to the file names.

LU 2.1 introduction

Introduction

Large part of the imprinted brain theory revolves around the dysfunctions in social behavior seen in people with ASD and PSD. The regulation of social behavior is currently best described in the social brain hypothesis. This hypothesis includes the different psychological processes involved in human social behaviour and the neural structures that regulate those processes. Aim of this self-study assignment and the subsequent meeting (3) is to gain more insight in the social brain hypothesis in general. Next week you will use this basic knowledge during self-study 4 (LU 3.2) and meeting 4 (LU 3.3) to gain a deeper understanding of the dysfunctions in social behavior in ASD and PSD and to discuss how the current insights about these dysfunctions relate to the imprinted brain theory.

Specific learning outcomes

- be able to explain the four areas of social cognition, i.e. recognizing others, recognizing oneself, controlling oneself and the interface between self and others, and the main psychological processes involved in these distinctive areas.
- Be able to name the main neural structures and networks that regulate aforementioned psychological processes.
- Be able to distinguish between automatic and controlled processes and their respective neural networks (X- versus C-system)

LU 2.2 Self-study assignment 3 - the social brain

Introduction

Aim of this self-study assignment and the subsequent meeting (3) is to gain more insight in the social brain hypothesis. i.e. how social cognitive functions are regulated by the brain, with a strong focus on functional neuroanatomy. To this end, you will read a key paper on the topic from Lieberman (2007, see resources below). The assignments and questions in this self-study assignment help you focus on the most important processes and brain structures.

Specific learning outcomes

- be able to explain the four areas of social cognition, i.e. recognizing others, recognizing oneself, controlling oneself and the interface between self and others, and the main psychological processes involved in these distinctive areas.
- Be able to name the main neural structures and networks that regulate aforementioned psychological processes.
- Be able to distinguish between automatic and controlled processes and their respective neural networks (X- versus C-system)

Literature

- Lieberman, M. Social cognitive neuroscience: a review of core processes. Ann Rev of Psychology 2007; 58:259-89. DOI: 10.1146/annurev.psych.58.110405.085654

Assignment 1: view this short knowledge videoclip to get acquainted with what we consider social cognition.

https://www.youtube.com/watch?v=H9lc-LZ_7dg

Assignment 2: The review paper from Lieberman (2007, see resources below) is considered one of the key papers within the field of social cognition. It describes the different psychological processes involved in human social behavior and the neural structures that regulate those processes that, together, encompass 'the social brain' hypothesis. Do not thoroughly read the overview paper from front to back but use it to answer the questions below. To get a first impression of the content, start by reading the abstract and the headers. In his paper, Lieberman distinguishes 4 main areas within social cognition: Understanding others,

understanding oneself, controlling oneself and processes directly related to interaction between self and others. Across these areas, he makes a distinction between automatic and controlled processes. Questions below are directed towards defining the main psychological processes relevant for these 4 core areas of social cognition and to get an overview of the neural structures involved in their regulation.

Questions:

Automatic versus controlled processes

1. What characteristics distinguish controlled processes from automatic processes?
2. The neural systems involved in automatic and controlled processes are referred to as the X-system and C-system. What brain regions are associated with both these systems?

Understanding others:

1. Two core processes are relevant to understand others, which are those?
2. What is 'theory of mind'? and why is it important in relation to social cognition?
3. What distinct functions are related to representing the mind of others? And what brain regions are involved? Try to specify what role each brain region plays.
4. What aspects of representing the mind of others are thought to be more or less automatic? And what aspects are considered a controlled process? Do the brain regions associated with these processes match with regions described for the X- and X-systems?
5. What distinct functions are related to experiencing the mental states of other? And what brain regions are involved? Try to specify what role each brain region plays.
6. To what extend is experiencing the mental states of other's and automatic or controlled process?

Understanding oneself:

1. What four core processes are relevant to understand oneself?
2. What distinct psychological processes are related to self-recognition? And what brain regions are involved? Try to specify what role each brain region plays.
3. What aspects of self-reflection can be distinguished? And what brain regions are involved? Try to specify what role each brain region plays.

Controlling oneself:

1. Why is self-regulation such an important aspect of social cognition?
2. What types of **intentional** self-regulation are described by Lieberman (2006)? And what brain regions are involved? Try to specify what role each brain region plays.
3. What types of **unintentional** self-regulation are described by Lieberman (2006)? And what brain regions are involved? Try to specify what role each brain region plays.
4. To what extend can automatic and controlled processed be distinguished? Do the brain regions associated with these processes match with regions described for the X- and X-systems?

Interface of self and others:

1. What role is described for mirror neurons and the psychological process of imitation in social cognition?
2. What other aspects of the interaction between self and others are distinguished and what brain regions seem to be important in these psychological concepts?
3. Lieberman describes the importance of social connection and social rejection. What changes in brain activity are related to social connection (being close to, or presented with an image of, a loved one)? What changes in brain activity are associated with social disconnection (e.g. being separated from a loved one).
4. What aspects of social decision making are distinguished by Lieberman (2006)? And what brain regions seem to be involved in these psychological processes?

Assignment 3

Summarize the main psychological processes and neural structures involved in a concept map, include at least the psychological processes mentioned in the learning outcomes. Bring your concept map to meeting 3.

Resources

Lieberman 2007.pdf

LU 2.3 Meeting 3 - The social brain

Introduction

During this meeting you will discuss the theory about the social brain you studied in self-study 3 and summarized in a concept map in small groups. In addition, you will discuss new experimental evidence and relate this to what you have already learned about the social brain.

Specific learning outcomes

- be able to explain the four areas of social cognition, i.e. recognizing others, recognizing oneself, controlling oneself and the interface between self and others, and the main psychological processes involved in these distinctive areas.
- Be able to name the main neural structures and networks that regulate aforementioned psychological processes.
- Be able to distinguish between automatic and controlled processes and their respective neural networks (X- versus C-system)

Literature

- Lieberman, M (2007). Social cognitive neuroscience: a review of core processes. Ann Rev of Psychology 58:259-89. DOI: 10.1146/annurev.psych.58.110405.085654
- Jauniaux J, Khatibi A, Rainville P, Jackson PL (2019). A meta-analysis of neuroimaging studies on pain empathy: investigating the role of visual information and observers' perspective. Social Cognitive and Affective Neuroscience 14(8):789-813

Part I: Understanding the social brain (20 minutes)

Assignment 1: work together in small groups and discuss the concept maps you prepared in self-study 3. Help each other to improve by filling in missing concepts and links.

Part II: Researching the social brain (60 minutes)

You will now study the results from a recent systematic review from Jauniaux et al (2019) that performed a meta-analysis of fMRI experiments on pain empathy.

Use this paper (see resources at bottom of page) for assignments 2 and 3. The abstract is already presented below to give a short overview of the paper and its main findings. Work together in small groups and make notes. At the end of the meeting some of you will be asked to discuss your findings during a group discussion.

Abstract

Empathy relies on brain systems that support the interaction between an observer's mental state and cues about the others' experience. Beyond the core brain areas typically activated in pain empathy studies (insular and anterior cingulate cortices), the diversity of paradigms used may reveal secondary networks that subserve other more specific processes. A coordinate-based meta-analysis of fMRI experiments on pain empathy was conducted to obtain activation likelihood estimates along three factors and seven conditions: visual cues (body parts, facial expressions), visuospatial (first-person, thirdperson), and cognitive (self-, stimuli-, other-oriented tasks) perspectives. The core network was found across cues and perspectives, and common activation was observed in higher-order visual areas. Body-parts distinctly activated areas related with sensorimotor processing (superior and inferior parietal lobules, anterior insula) while facial expression distinctly involved the inferior frontal gyrus. Self- compared to other-perspective produced distinct activations in the left insula while stimulus- versus other-perspective produced distinctive responses in the inferior frontal and parietal lobules, precentral gyrus, and cerebellum. Pain empathy relies on a core network which is modulated by several secondary networks. The involvement of the latter seems to depend on the visual cues available and the observer's mental state that can be influenced by specific instructions.

Key words: Pain empathy; fMRI; Meta-analysis; Activation Likelihood Estimate; Perspective-taking; Visual information

Assignment 2: **Incorporating new evidence**

1. What brain regions showed activation when data was analyzed across all pain empathy experiments? Do you see overlap with the neural structures discussed in Lieberman (2007). If so, what structures? And did Lieberman's overview also link these structures to empathy?
2. In their paper, Jauniaux et al. distinguish three factors related to empathy, namely visual cues, visuospatial and cognitive perspectives. Try to explain what the contribution of these factors is to empathy.
3. Separate analyses were done for brain activation specifically related to visual cues, visuospatial perspective and cognitive perspective. What brain regions are involved in these specific aspects of empathy? Make a short overview.
4. Above questions have helped you to elaborate on what you have learned during SS3 about the relevant psychological processes and neural structures underlying empathy. Now try to complement that part of the concept map with more detailed information on the regulatory processes and neural structures underlying empathy, as summarized in questions 1 to 3.

Assignment 3: Based on the papers from Lieberman (2007) and Jauniaux et al (2019), what is still unknown about the psychological processes underlying empathy and the neural structures involved in their regulation? Select at least two examples and take them to group discussion.

Group discussion Part II (20 minutes)

Resources

Jauniaux et al 2019.pdf

Week 3 The social brain in ASD and PSD

LU P3.1 Consultation meeting

Preparation consultation meeting

Read and critically discuss the feedback your received from your fellow students and project supervisor within your project group.

Prepare an overview of issues that you still have questions about in relation to the research question you formulated and upload to this overview to the files section of your MS teams project-groupchannel before February 22nd, midnight.

On February 23rd, you will have a 20-minutes consultation meeting with your project supervisor. This meeting will be scheduled within the time slot 13:15-15:00 hours. Exact time of your meeting will be announced within your project-group channel.

LU P3.2 Literature research disciplinary grounding

Literature research

Assignment

1 Discuss your strategy to divide the work for the literature survey. In principle, each student focuses on 1 discipline during this literature research phase of the project.

2 Every student should at least read and analyze 4 scientific papers/articles and add the findings to the Data Management Table (DMT, see below).

3 Starting up a literature study with only limited background knowledge is really difficult. The easiest way to get started is to read some easy understandable (popular science or textbook) literature on the topic.

4 The next step is to search for relevant literature reviews and research articles on the topic. Below you find some suggestions for relevant literature databases. Additional suggestions can be found on the website of Utrecht University library (https://www.uu.nl/en/university-library/searching-for-literature/search-engines-by-discipline)

- Scopus: https://www.scopus.com
- PubMed https://www.ncbi.nlm.nih.gov/pubmed
- Web of Science: https://apps.webofknowledge.com

5 Once you have identified the most relevant literature, it is helpful to make a data-management table (DMT, see below). A DMT not only provides an overview of the relevant disciplinary insights, it will also help you in the next phase of the project where you will try to find common ground.

6 Each student makes an individual DMT and after discussing your findings (meeting April 1st, LU P8.1), you put all the information together and create one DMT per project group. More information about the use of a DMT, see *An Introduction to Interdisciplinary Research : Theory and Practice*,pag.71-77.

TIP Of course, you must reassure that you have read relevant literature, but think for yourself before you start an extensive literature survey. Brainstorm

with your fellow students, and design a preliminary mindmap, containing the most relevant insights. Another good starting point is to interview an expert.

Searching relevant literature – information literacy skills

Information literacy skills help you to find, evaluate and process scientific information. After completing this **two-hour training**, you will have acquired the necessary skills to effectively conduct your literature survey for your project. https://www.uu.nl/en/university-library/help-in-searching/information-literacy-skills/compass

Data management table

Helpful sources of information at the start of your literature research are review articles. Once you have identified the most relevant literature, it is helpful to make a data-management table, see below. A data-management table not only provides an overview of the relevant disciplinary insights, but it will also help you in trying to find common ground.

Full reference to the book or article:			
Discipline/ sub-discipline:			
Theory/hypothesis	**Research question**	**methodology**	**Results & implications**
What theory lies at the basis of this article/subject?	What was the research question they tried to answer in this article?	What methodology / experimental design was used to answer the research question?	What were the main results described in the paper and what implications do these results have in the context of your own research question?

Adapted from: Data-management table as developed by Menken & Keestra (2016). An introduction to Interdisciplinary research; theory and practice.

LU 3.1 Introduction

Introduction

In their imprinted brain theory, Crespi and Badcock hypothesize that autism spectrum disorder and psychotic spectrum disorder represent "*two extremes of a cognitive spectrum with normality in its center*", with social cognition being underdeveloped in ASD and hyper-developed in PSD (Crespi & Badcock, 2008). Recently, Fernandes et al (2018) performed a systematic review of literature on performance of ASD and PSD subjects on social cognitive tasks. This week, you will compare the data presented in this paper to the evidence provided by Badcock & Crespi (2008) and use this data to investigate to what extend this hypothesis is currently still supported by the latest scientific evidence.

Specific learning outcomes

- State the most prominent deficits in social cognition in autism spectrum disorders.
- State the most prominent deficits in social cognition in psychotic spectrum disorders.
- Link experimental evidence from literature to current knowledge about social cognitive deficits in ASD and PSD.
- Critically evaluate the imprinted brain theory from a psychological perspective with the use of scientific arguments.

LU 3.2 Self-study assignment 4 - the social brain in ASD and PSD

Introduction

During this self-study you will gather the most relevant information from Fernandes's systematic review on the performance of ASD and PSD subjects on social cognitive tasks. In addition, you will summarize the most important differences between ASD and PSD presented in this review. Finally, you will compare these findings to the evidence presented by Badcock & Crespi (2008). During meeting 4 you will discuss all evidence and draw a conclusion about the question to what extend this hypothesis is currently still supported by the latest scientific evidence.

Specific learning outcomes

- State the most prominent deficits in social cognition in autism spectrum disorders.
- State the most prominent deficits in social cognition in psychotic spectrum disorders.
- Link experimental evidence from literature to current knowledge about social cognitive deficits in ASD and PSD.
- Critically evaluate the imprinted brain theory from a psychological perspective with the use of scientific arguments.

Literature

- Fernandes JM, Cajão R, Lopes R, Jerónimo R and Barahona-Corrêa JB (2018). Social Cognition in Schizophrenia and Autism Spectrum Disorders: A Systematic Review and Meta-Analysis of Direct Comparisons. Front. Psychiatry 9:504. doi: 10.3389/fpsyt.2018.00504
- Crespi B, Badcock C (2008) Psychosis and autism as diametrical disorders of the social brain. Behavioral and Brain Sciences 31: 241-320

Assignment 1 - Clinical presentation of social cognitive deficits

Look back at self-studies 1 and 2 and the insights you gained during SS3 and meeting 3: What characteristics and symptoms of ASD and PSD are related to the social brain?

In the introduction, Fernandes et al present the most commonly described domains in which ASD and PSD subjects show deficits. Provide the specific

domains for both ASD and PSD, as described in Fernandes et al. Is this overview consistent with the social deficits discussed during meeting 2?

Experimentally evaluating social cognition.

Assignment 2

watch web clips from Carlijn van den Boomen (follow link below) about her research on perception of social cues in subjects with autistic spectrum disorder.

web clips Carlijn van den Boomen

Try to link the processes she discusses to the processes you included in your concept map from self-study 3. We will discuss this in more detail during meeting 4.

Assignment 3

Fernandes et al 2018 selected data from psychometric outcome measures that were classified according to 4 different dimensions: 1. Emotional perception; 2. Theory of mind; 3. Emotional intelligence and 4. Social skills. The tasks used to assess these dimensions are presented in table 1 of the paper. Try to find information on what exactly is measured during these tasks and what they tell you about the respective social cognition dimensions. **A joint file is available in which you can collectively gather the necessary information.**

Assignment 4 – Comparison between ASD and PSD

Fernandes et al 2020 investigated to what extent social deficits in ASD could be differentiated from those in PSD. Use the questions below to get an overview of the main results from the systematic review.

1. What differences are reported between ASD and PSD with respect to **emotional perception**? For what specific outcome measures where these differences detected? Results are summarized in Figures 2 and 3.
2. What differences are reported between ASD and PSD with respect to **theory of mind**? For what specific outcome measures where these differences detected? Results are summarized in figures 4, 5 and 6.
3. What differences are reported between ASD and PSD with respect to **emotional intelligence and social skills**? For what specific outcome measures where these differences detected? Results are summarized in figure 7.

4. What is the main conclusion Fernandes et al. draw in relation to the comparison in social cognitive deficits in ASD and FSD?

Assignment 5 – Crespi & Badcock's imprinted brain theory

In their overview paper from 2008, Crespi and Badcock provide an overview of the evidence supporting their theory. This evidence is summarized in table 1 and discussed in detail in the body text, chapter 6. Highlight the evidence that is directly related to social cognition (table 1, more details in body text, paragraphs 6.3 and 6.4), and compare these findings to the results from Fernandes et al (2018). Indicate overlap and contradictions.

You will use the information you gathered in this self-study in group discussion during **meeting 4.**

Resources

Crespi Badcock 2008 - review imprinted brain theory.pdf
Fernandes et al 2018 social cognition SR.PDF
slides web clips Carlijn van den Boomen.pdf

LU 3.3 Meeting 4 - Imprinted brain theory from a psychological perspective

Introduction

In their imprinted brain theory, Crespi and Badcock hypothesize that the autism spectrum disorder and psychotic spectrum disorder represent "*two extremes of a cognitive spectrum with normality in its center*", with social cognition being underdeveloped in ASD and hyper-developed in PSD (Crespi & Badcock, 2008). In self-study 4, you studied the main findings from the systematic review by Fernandes et al (2018) on the performance of ASD and PSD subjects on social cognitive tasks. Today we will directly compare the evidence presented in this paper to the evidence brought forward by Crespi & Badcock. In addition, we will provide evidence from a follow-up study that directly compared the social cognitive performance of ASD and PSD subjects (Pinkham et al 2020). At the end of the meeting, you will have formed an evidence-based view on the question to what extend this hypothesis is currently still supported by the latest scientific evidence.

Specific learning outcomes

- State the most prominent deficits in social cognition in autism spectrum disorders.
- State the most prominent deficits in social cognition in psychotic spectrum disorders.
- Link experimental evidence from literature to current knowledge about social cognitive deficits in ASD and PSD.
- Critically evaluate the imprinted brain theory from a psychological perspective with the use of scientific arguments.

Literature

- Fernandes JM, Cajão R, Lopes R, Jerónimo R and Barahona-Corrêa JB (2018). Social Cognition in Schizophrenia and Autism Spectrum Disorders: A Systematic Review and Meta-Analysis of Direct Comparisons. Front. Psychiatry 9:504. doi: 10.3389/fpsyt.2018.00504
- Crespi B, Badcock C (2008) Psychosis and autism as diametrical disorders of the social brain. Behavioral and Brain Sciences 31: 241-320
- Pinkham AE, Morrison KE, Penn DL, Harvey PD, Kelsven S, Ludwig K, Sasson NJ (2020). Comprehensive comparison of social cognitive performance in autism spectrum disorder and

schizophrenia. Psychological Medicine 50, 2557–2565. https://doi.org/10.1017/S0033291719002708

General instruction

Work in your peer-tutoring groups on the assignments below. In assignment 1 and 2, you will summarize all the relevant evidence gathered during the self-study assignment. In the second part of the meeting, information will be combined to collect all the evidence from psychology that support and oppose Crespi & Badcock's theory.

Assignment 1

Collect all the arguments (experimental evidence) from Fernandes et al (2018) and Crespi & Badcock (2008) that support or oppose the hypothesis that social cognition is underdeveloped in ASD and hyper-developed in PSD and these deficits are, thus, two extremes of a continuum. Also include the evidence presented in Carlijn van den Boomen's web clips. Most of the evidence you already collected during self-study 4. Try to elaborate on the evidence, by also providing the concrete experimental results that were discussed.

Assignment 2

On basis of the main results in the systematic review from Fernandes et al (2018), Pinkham et al. decided to do a follow-up study in which they directly compared social cognitive performance of ASD and PSD subjects to each other and to a typically developing (TD) control group. The results are presented in Pinkham et al (2020, see resources). The table below gives an overview of the results.

1. On what aspects of social cognition do ASD and PSD differ from typically developing controls?
2. On what aspects of social cognition do ASD and PSD differ from each other?
3. Compare the findings described in a. and b. to the evidence you already summarized in your concept map from self-study assignment 4. Do the findings provide additional evidence to existing arguments or do they introduce new arguments? Incorporate in your concept maps.

Table 2. Social cognitive performance

Task (possible range)	TD ($n = 101$) mean (s.d.)	ASD ($n = 101$) mean (s.d.)	SCZ ($n = 92$) mean (s.d.)	$d_{TD\ v.\ ASD}$	$d_{TD\ v.\ SCZ}$	$d_{ASD\ v.\ SCZ}$	$p_{group\ main\ effect}$	Direction
Attributions								
AIHQ – Aggression bias (1–5)	1.89 (0.39)	1.92 (0.42)	1.86 (0.36)	0.07	0.08	0.15	0.37	–
AIHQ – Blame score (3–16)	7.67 (3.23)	7.52 (3.45)	8.19 (2.97)	0.04	0.17	0.21	0.13	–
AIHQ – Hostility bias (1–5)	1.92 (0.82)	2.03 (0.88)	2.29 (0.76)	0.13	**0.47**	**0.32**	**<0.001**	SCZ > TD, ASD
Emotion recognition								
BLERT Total score (0–21)	17.24 (4.08)	16.14 (4.36)	15.67 (3.76)	**0.26**	**0.40**	0.12	**0.001**	TD > ASD, SCZ
Anger (0–3)	2.55 (0.97)	2.53 (1.05)	2.31 (0.90)	0.02	0.26	0.22	0.04	–
Disgust (0–3)	2.17 (1.18)	2.03 (1.26)	2.00 (1.08)	0.11	0.15	0.03	0.29	–
Fear (0–3)	1.86 (1.19)	1.72 (1.27)	1.64 (1.09)	0.11	0.19	0.07	0.19	–
Happy (0–3)	2.74 (0.82)	2.72 (0.88)	2.55 (0.76)	0.02	0.24	0.21	0.05	–
Neutral (0–3)	2.60 (0.93)	2.44 (0.99)	2.45 (0.86)	0.17	0.17	0.01	0.14	–
Sad (0–3)	2.71 (1.06)	2.39 (1.13)	2.35 (0.97)	**0.29**	**0.35**	0.04	**0.001**	TD > ASD, SCZ
Surprise (0–3)	2.61 (1.03)	2.33 (1.10)	2.38 (0.95)	0.26	0.23	0.05	0.012	–
ER-40 Total score (0–40)	33.15 (5.73)	31.45 (6.13)	30.93 (5.28)	**0.29**	**0.40**	0.09	**<0.001**	TD > ASD, SCZ
Anger (0–8)	5.32 (2.11)	4.89 (2.25)	5.11 (1.95)	0.20	0.10	0.10	0.130	–
Fear (0–8)	6.57 (2.19)	6.13 (2.34)	5.68 (2.02)	0.19	**0.42**	0.21	**0.001**	TD > SCZ
Happy (0–8)	7.83 (1.02)	7.65 (1.09)	7.68 (0.94)	0.17	0.15	0.03	0.164	–
Neutral (0–8)	6.41 (2.58)	6.36 (2.75)	5.58 (2.38)	0.02	**0.33**	**0.30**	**0.003**	TD, ASD > SCZ
Sad (0–8)	7.03 (1.77)	6.41 (1.90)	6.87 (1.64)	**0.34**	0.09	**0.26**	**0.002**	TD, SCZ > ASD
EmoBio Total score (0–1)[a]	0.88 (0.17)	0.81 (0.18)	0.78 (0.15)	**0.40**	**0.62**	0.18	**<0.001**	TD > ASD, SCZ
Anger (0–1)	0.85 (0.24)	0.79 (0.26)	0.79 (0.22)	**0.24**	**0.26**	0.00	**0.008**	TD > ASD, SCZ
Fear (0–1)	0.87 (0.30)	0.78 (0.32)	0.68 (0.27)	**0.29**	**0.67**	**0.34**	**<0.001**	TD > ASD > SCZ
Happy (0–1)	0.85 (0.22)	0.76 (0.23)	0.81 (0.19)	**0.40**	0.19	0.24	**<0.001**	TD > ASD
Neutral (0–1)	0.89 (0.28)	0.86 (0.30)	0.80 (0.26)	0.10	**0.33**	0.21	**0.006**	TD > SCZ
Sad (0–1)	0.92 (0.26)	0.85 (0.28)	0.83 (0.24)	**0.26**	**0.36**	0.08	**0.003**	TD > ASD, SCZ
Social perception								
Benton (0–54)[a]	46.33 (6.10)	43.29 (6.49)	44.89 (5.46)	**0.48**	0.25	**0.27**	**<0.001**	TD, SCZ > ASD
Bio Motion (n/a)[a]	2.56 (1.21)	2.48 (1.28)	2.25 (1.07)	0.06	0.27	0.19	0.05	–
RAD (0–45)[a]	33.19 (7.79)	30.22 (8.33)	30.10 (7.09)	**0.37**	**0.41**	0.02	**<0.001**	TD > ASD, SCZ
Mental state attribution								
CToM Intentions (0–14)[a]	11.27 (3.53)	11.27 (3.75)	10.66 (3.16)	0.00	0.18	0.18	0.193	–
Eyes (0–36)[a]	25.45 (6.51)	22.80 (6.88)	22.84 (6.02)	**0.40**	**0.42**	0.01	**<0.001**	TD > ASD, SCZ
Hinting (0–20)	17.31 (4.49)	14.57 (4.80)	14.63 (4.15)	**0.59**	**0.62**	0.01	**<0.001**	TD > ASD, SCZ
TASIT Total score (0–64)	55.37 (9.61)	48.22 (10.27)	49.88 (8.88)	**0.72**	**0.59**	0.17	**<0.001**	TD > ASD, SCZ
Lies (0–32)	28.36 (5.83)	24.05 (6.23)	25.73 (5.38)	**0.71**	**0.47**	**0.29**	**<0.001**	TD > SCZ > ASD
Sarcasm (0–32)	27.01 (6.10)	24.27 (6.52)	24.15 (5.63)	**0.43**	**0.49**	0.02	**<0.001**	TD > ASD, SCZ
Additional measure								
Trust Total score (−3 to +3)[a]	0.38 (1.11)	.21 (1.16)	0.13 (1.02)	0.15	0.23	0.07	0.06	–
Trustworthy (−3 to +3)	1.36 (1.33)	0.98 (1.40)	0.94 (1.23)	**0.28**	**0.33**	0.03	**0.003**	TD > ASD, SCZ
Untrustworthy (−3 to +3)	−0.51 (1.13)	−0.50 (1.19)	−0.61 (1.04)	0.01	0.09	0.10	0.61	–

TD, typically developing; ASD, autism spectrum disorder, SCZ, schizophrenia.

Note: Means are presented as estimated marginal means from models accounting for age, gender, and race. Bolded values indicate statistical significance. Main effects of group are statistically significant if $p < 0.01$, and pairwise group comparisons were evaluated for statistical significance at the Bonferroni-corrected value of $p < 0.0167$.

[a]Sample sizes vary for these analyses. They are as follows: EmoBio: TD = 101, ASD = 101, SCZ = 78; Benton and CToM Intentions: TD = 101, ASD = 101, SCZ = 79; Bio Motion: TD = 93, ASD = 96, SCZ = 73; RAD: TD = 101, ASD = 101, SCZ = 89; Eyes and Trust: TD = 101, ASD = 98, SCZ = 92.

Assignment 3

Work together in your peer-tutoring groups in creating a final overview that summarizes the following:

1. On what aspects do ASD and PSD differ from healthy subjects?
2. On what aspects do ASD and PSD differ from each other?
3. To what extent can you argue that these deficits represent to extremes from one continuum? What arguments support, and what arguments oppose, this statement

Add your answers to question 3 and the three most important arguments that led to this answer to the summary tabel in the "BA219 meeting 4 evidence" file (folder 'meeting 4'). We will use this for general discussion.

General discussion

Some of you will be asked to discuss their summaries of conclusion and most important arguments during group discussion. On basis of these summaries we will discuss the current state of evidence in relation to the psychological aspects of the imprinted brain theory.

Resources

Pinkham et al 2020.pdf

Week 4 Neurobiology of ASD and PSD

LU 4.1 Introduction

Introduction

As discussed earlier, although autism and psychosis seem totally unrelated disorders and are described in different categories in psychology text books, researchers Christopher Badcock and Bernard Crespi have put forward a theory* which states that autism and psychosis represent extremes of a continuum of behavioural traits, making these disorders diametrically opposed to each other.

This week we will focus on the neurobiological perspective of this imprinted brain theory. As most evidence linking both diseases currently stems from changes in neuronal growth and neuroanatomy, this will be the focus.

For students without any background knowledge on how the brain works, we highly recommend to study LU 4.2 (Catch up neurobiology) before continuing with the LU 4.3 (self-study 6).

Learning outcomes

After the learning activities within this theme, you should be able to:

- Explain how synapse formation and synaptic pruning contribute to brain development.
- Describe the differences in synapse formation and synaptic pruning associated with altered brain development in ASD and PSD.
- Critically evaluate the scientific evidence related to the neurobiological perspective of the imprinted brain theory.

LU 4.2 Self-study 5 Catch up neurobiology (ELECTIVE)

SELF-STUDY 5 Basic neurophysiology for students without background knowledge about central nervous system.

Introduction

This learning unit is specifically aimed at students with a different disciplinary background than biology, neuroscience, or pharmacy. This learning unit helps you to attain a basic understanding of how the brain works on a neuronal level. This will help you better understand pathophysiology and putative role of genetic imprinting in autistic spectrum disorder and psychotic spectrum disorder. This unit discusses two different topics:

1.Basics of neuronal communication: neurotransmission

2.Modulation of neurotransmission by psychoactive compounds

This will hopefully help you better understand the content of the upcoming meetings.

Learning outcomes

After this self-study you will be able to:

- Describe the chemical processes that are responsible for the generation of action potentials.
- Explain the role of neurotransmitters in communication between neurons.
- Explain how the level of neurotransmission can be influenced by psychoactive drugs

1. Basics of neuronal communication: neurotransmission

All cells maintain a membrane potential under resting conditions. This so called 'resting' membrane potential is essential for a regulated propagation of signals through neurons. In neurons, this resting membrane potential isaround -65mV. Signal transduction through neurons is mediated

by action potentials. During an action potential, this membrane potential quickly rises through opening of sodium channels.

The following movie explains how an action potential is generated.

https://www.youtube.com/watch?v=BbUcWbtVjT4

Communication between neurons depends mainly on the release of neurotransmitters into a synapse and subsequent binding of those neurotransmitters to receptors on the postsynaptic membrane. The release of these neurotransmitters is induced by action potentials arriving at the presynaptic nerve terminal. The following movie explains the release of neurotransmitters step by step.

https://www.youtube.com/watch?v=Ac-Npt3vgCE

With about 10^{14} synaptic connections, communication within the brain is extremely complex and requires strong regulation. This regulation is accomplished at different levels, a.o. at the level of neurotransmitter and receptor interaction and at the level of organized neuronal networks. A variety of different neurotransmitters exists that all act on their own set of specific receptors. Different neurons release different neurotransmitters, creating specificity of signals within neuronal networks. The following video gives an extensive description of the different (types of) neurotransmitters in the brain.

https://www.youtube.com/watch?v=FXYX_ksRwIk

Within one neurotransmitter system, different effects can be established depending on the specific receptor that is expressed on the postsynaptic membrane. For example, dopamine can bind to two different receptors, the D1 and the D2 receptor. Both receptors are G-protein coupled receptors. However, whereas D1 receptors are coupled to Gs proteins and activation of these receptors results in activation and depolarization of the neuron, D2 receptors are coupled to Gi proteins and activation of these receptors results in inhibition and hyperpolarization of the neuron. The following video gives an overview of different types of receptors and explains how these different receptors affect neuronal activity.

https://www.youtube.com/watch?v=yg44T2HcA2o

2. Modulation of neurotransmission by psychoactive compounds

Neuronal activity within a neuronal network can be pharmacologically modulated in different ways. You could, for example, pharmacologically modulate resting membrane potential or the generation of action potentials, but you could also modulate the signal transduction between neurons (i.e. neurotransmission). The mechanism of action of different anti-epileptic compounds very nicely illustrates all these
different ways of modulating neurotransmission.

The following video gives an overview of different mechanisms of action of anti-epileptic drugs.

https://www.youtube.com/watch?v=xFUHE9gX6W8

This self-study illustrated the primary way of communication between neurons. The effectiveness of communication within a neural network depends on the localization and number of connections between neurons (i.e. synapses). It has been hypothesized that altered synapse formation during development may at least partly explain the pathophysiology of both ASD and PSD. That's why we will focus on this aspect of brain development in the upcoming meetings.

LU 4.3 Self-test Catch up neurobiology (ELECTIVE)

Changes in membrane potential during an action potential result from changes in permeability of different specific ion channels. Which of the statements below is true for the refractory period?

a. Na+ channels are closed, K+ channels are open
b. Na+ channels are open, K+ channels are closed
c. Both Na+ channels and K+ channels are closed
d. Both Na+ channels and K+ channels are open

How does an action potential travel across the axon?

a. By activation of Na+/K+ proteins
b. By activation of voltage-gated Ca2+ channels
c. By activation of voltage-gated Na+ channels
d. By activation of ligand-gated Na+ channels

What mechanism does not prolong the chemical signaling of neurotransmitters?

a. Inhibition of the presynaptic autoreceptor
b. blockade of the re-uptake transporter
c. Synaptic degradation of the neurotransmitter
d. Activation of presynaptic Ca2+ channels

What statement about AMPA receptors is true?

a. AMPA receptors are ionotropic receptors that are G-protein coupled and induce a slow effect after activation.
b. AMPA receptors are metabotropic receptors that are G-protein coupled and induce a fast effect after activation.
c. AMPA receptors are ionotropic receptors that are ion-channel coupled and induce a slow effect after activation.
d. AMPA receptors are ionotropic receptors that are ion-channel coupled and induce a fast effect after activation.

What is the most important trigger for the release of vesicles in the synapse

a. resting potential
b. intracellular calcium concentration
c. actionpotential
d. extracellular calcium concentration

LU 4.4 Self-study assignment 6 - neuroplasticity

Introduction

From a psychiatric perspective, a lot of emphasis is put on the dopamine hypothesis op psychosis, i.e. hyperexcitability of the mesolimbic dopamine system is responsible for the positive symptoms of schizophrenia and these can be treated by normalizing this overflow of dopaminergic signaling with D2 receptor antagonists. For autism spectrum disorder, very little is known about the underlying neurophysiological cause. One thing that connects both diseases is the hypothesis that altered synapse formation during development may at least partly explain the pathophysiology of both ASD and PSD. That's why we will focus on this aspect of brain development in the upcoming meetings.

Learning outcomes:

After this self-study assignment, you should be able to

- Explain the phrase 'use it or lose it' in the context of neuroplasticity.
- Explain the difference between synaptic plasticity and structural plasticity.
- Describe the cellular mechanisms responsible for neuroplasticity.
- Describe how synaptic sprouting and synaptic pruning contribute to neurodevelopment.
- Describe the differences in synapse formation and synaptic pruning associated with altered brain development in ASD and PSD.

Literature:

Forrest, Parnell and Penzes (Nature Review Neurosci; 2018; 19:215-234; ***DOI*** *10.1038/nrn.2018.16).*

Neuroplasticity

Cognitive functions are embedded in neuronal circuits in the brain. These neuronal circuits are not static, they are shaped during early development and refined throughout adulthood. These adaptations are referred to as structural plasticity. Two important processes involved in this structural plasticity are synaptic sprouting and synaptic pruning, the processes in which connections between neurons are strengthened or weakened, respectively, in an activity-dependent manner. The next video explains these structural changes in connectivity, illustrating both synaptic sprouting and synaptic pruning. In addition, it makes an explicit distinction between structural plasticity and

synaptic plasticity. In literature, however, synaptic plasticity is also regularly considered a form of structural plasticity.

https://www.youtube.com/watch?v=J8wW1t1JqUc

Research implies that specific changes in the number of spines (i.e. synaptic connections), caused by a change in the balance between synaptic sprouting and synaptic pruning, may actually underly neurological and psychiatric diseases, including autism spectrum disorder and psychotic spectrum disorder. To study structural plasticity and its link to psychiatric disease in more detail, we will use a very illustrative review from Forrest, Parnell and Penzes (Nature Review Neurosci; 2018; 19:215-234; **DOI** 10.1038/nrn.2018.16, see resources at bottom of the page). This review gives an overview of mechanisms involved in structural plasticity and provides an in-depth explanation of how changes in gene expression may relate to changes in structural plasticity and the development of psychiatric disease. During this, and upcoming, learning activities we will study and discuss several parts of this review and link this to what we have already learned about the social brain and ASD and PSD.

Assignments

Read the first pages of the paper (till *Atypical spine and dendrite development*). And answer the following questions:

1) The paper states that structural plasticity of cortical pyramidal neurons in the neocortex is of particular interest for neuropsychiatric disorders like autism spectrum disorder and psychotic spectrum disorder. Do you agree with this? Use what you have learned about pathophysiology of both diseases and about the social brain to explain your answer.

2) Can you tell something about the dynamics of dendritic branches and dendritic spines throughout development?

3) Provide a general description of the balance between synaptic sprouting and pruning throughout development on basis of Figure 1.

Figure 2 gives a general overview of neuronal mechanisms responsible for structural plasticity. Two types of structural plasticity are distinguished, which are Hebbian synaptic plasticity and homeostatic plasticity. Questions:

4) What is the difference between Hebbian synaptic plasticity and homeostatic plasticity?

5) What determines whether a spine grows? And what determines whether a spine shrinks? Explain what cellular processes are involved.

6) In the context of plasticity, an often-used phrase is '*use it or lose it*'. Explain this phrase.

7) Read the paragraph about spine pathology in autism spectrum disorder and explain the current hypothesis on this topic.

8) Read the paragraph about spine pathology in schizophrenia and explain the current hypothesis on this topic.

Several variations have been found in genes involved in structural plasticity. Some of those variations have been associated with an increased risk of ASD, PSD or both. **Table 1** and **figure 3** give an overview of identified risk loci, the role of those genes in structural plasticity and the biological pathways they are involved in.

9) During meeting 6 we will discuss different groups of risk loci (see table 1, Forrest et al 2018). Check what topic you will have to discuss in your peer-tutoring group during meeting 6 and read the paragraphs from Forrest et al (2018) relevant for that topic:

1. Paragraph on respective topic in section "genetic risk and structural plasticity" including figure 3.
2. Paragraph on respective topic in section "Novel therapeutic avenues" including figure 4.

Group	**Functional group of neuropsychiatric risk loci (table 1)**
1	Glutamate receptors
2	Calcium signaling
3	GTPase signaling
4	Glutamate receptors
5	Calcium signaling
6	GTPase signaling
7	Glutamate receptors

Resources

Forrest et al 2018.pdf

LU 4.5 Apply neuroplasticity to ASD and PSD

Introduction

From self-study assignment 6 you have learned that both ASD and PSD are associated with changes in structural plasticity. In addition, several variations have been found in genes involved in structural plasticity of which some have been associated with an increased risk of ASD, PSD or both. **Table 1** and **figure 3** from Forrest et al (2018) give an overview of identified risk loci, the role of those genes in structural plasticity and the biological pathways they are involved in. During this meeting we will try to explain the normal function of these neuropsychiatric risk loci and make the functional link to their putative roles in neuroplasticity deficits in ASD and PSD. We will also discuss putative pharmacological treatment.

Literature:

- Forrest, Parnell and Penzes (Nature Review Neurosci; 2018; 19:215-234; **DOI** 10.1038/nrn.2018.16).

Assignment 1 Group discussion self-study assignment 6 (15 minutes)

We will use mentimeter to check your understanding of the concepts discussed in self-study assignment 6 and use this as input for further explanation.

Assignment 2 functional explanation of risk loci (60 minutes).

In this assignment you will try to explain the normal function of the assigned neuropsychiatric risk loci and make the functional link to their putative roles in neuroplasticity deficits in ASD and PSD. You will also looking at putative pharmacological treatment targeting those loci.

- Discuss in you peer-tutoring group how each of the proteins mentioned for 'your' functional group of neuropsychiatric risk loci is normally involved in structural plasticity.
- Discuss, on basis of information in Forrest et al (2018), how changes in these proteins could be involved in the development of ASD and PSD. You can look up the sources mentioned in Forrest et al for additional information.
- Make (or adapt) a drawing which you can use during general discussion to illustrate the potential pathological mechanism
- Discuss how the proteins in 'your' functional group of neuropsychiatric risk loci could be targeted to potentially overcome ASD and/or PSD. In corporate this in your drawing.

Group	Functional group of neuropsychiatric risk loci (table 1)
1	Glutamate receptors
2	Calcium signaling
3	GTPase signaling
4	Glutamate receptors
5	Calcium signaling
6	GTPase signaling
7	Glutamate receptors

Relevant parts of Forrest et al 2018 for this assignment:

1. Paragraph on respective topic in section “genetic risk and structural plasticity” including figure 3.
2. Paragraph on respective topic in section “Novel therapeutic avenues” including figure 4.

General discussion (30 minutes)

Several groups will be asked to discuss the functional role of their assigned risk loci, explain how they might be involved in the pathology of ASD and PSD and discuss how they could be targeted with drugs to overcome the deficits seen in ASD and PSD.

LU 4.6 Self-study assignment 7 - Neurobiological deficits in ASD and PSD

Introduction

During the previous meeting we focused on structural and genetic evidence related to the neurobiological perspective of the imprinted brain theory. In self-study assignment 7 and meeting 7, we will focus on the signaling pathways involved in neuronal plasticity.

Literature:

- Crespi B, Badcock C (2008) Psychosis and autism as diametrical disorders of the social brain. Behavioral and Brain Sciences 31: 241-320
- Lieff, J. The very intelligent protein mTOR. Published 01-18-2015, last accessed 02-23-2021. https://jonlieffmd.com/blog/intelligent-protein-mtor

Assignment 1

Crespi & Badcock discuss neurodevelopmental evidence for their imprinted brain theory in paragraph 6.2. Read this paragraph and summarize the arguments supporting and opposing the theory.

Assignment 2

In meeting 7, we will discuss an additional line of evidence related to signaling pathways involved in neuroplasticity, which focuses on the mammalian Target Of Rapamycin (mTOR) pathway. To be able to understand the provided literature on the role of mTOR in both autism spectrum disorder and psychotic spectrum disorder, it is important to understand mTOR's normal role in neuronal processes. To this end, read the popular science paper by Jon Lieff, MD (see link below). After reading this paper, you should be able to use the schemes below to explain how mTOR is involved in neuroplasticity. More specifically, you should be able to explain:

- What pathways regulate mTOR activity.
- How activation of mTOR contributes to neuronal growth.

Link to paper by Jon Lieff, MD: https://jonlieffmd.com/blog/intelligent-protein-mtor

Schemes describing mTOR pathway and physiological function (taken from Switon et al 2016,
Neuroscience http://dx.doi.org/10.1016/j.neuroscience.2016.11.017):

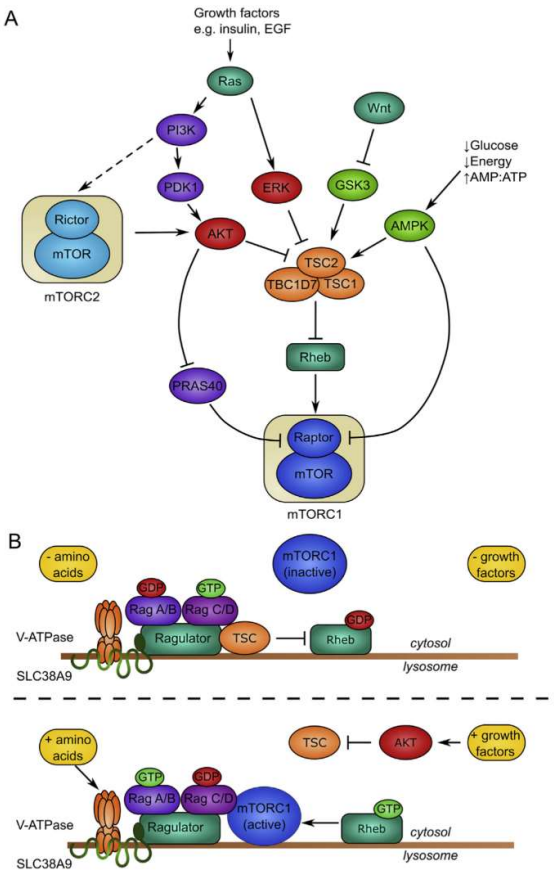


Fig. 2. Regulators of mTOR activity. (A) TSC1/2-dependent and -independent pathways of mTORCs regulation by trophic factors, glucose and cellular energy levels. The canonical pathway of mTORC1 activation by trophic factors starts with the activation of their respective receptor tyrosine kinases and subsequent increase in PI3K-Akt and ERK signaling. Akt and ERK inactivate TSC complex, which is a major inhibitor of mTORC1. However, when cellular energy level is low TSC is activated by AMPK, what prevents response to trophic factors. Some kinases can also regulate mTORC1 directly. Akt phosphorylates and inactivates PRAS40, leading to mTORC1 activation. In contrast, AMPK phosphorylates Raptor, leading to mTORC1 inactivation. Trophic factors can also activate mTORC2 via PI3K. (B) mTORC1 regulation by amino acids. The key component of mTORC1 regulation by amino acids is Rag–Ragulator complex. This complex consists of small Rag GTPases, which form heterodimers that contain RagA or RagB with RagC or RagD, and the Ragulator complex, consisting of five proteins: p18, p14, MEK partner 1 (MP1), hepatitis B virus X-interacting protein (HBXIP), and c7orf59. The RagA/B and RagC/D heterodimers are tethered to the cytoplasmic surface of the lysosome by the Ragulator scaffold. In amino acid-starved cells, RagA/B binds GDP, and RagC/D binds GTP, and the complex is unable to recruit mTORC1 to the lysosome. Upon the addition of amino acids, the dimers change their nucleotide-binding state to RagA/B-binding GTP and RagC/D-binding GDP. This "active" dimer binds Raptor and recruits mTORC1 to the lysosomal surface for subsequent activation by Rheb. The Ragulator complex serves as a scaffold for Rag GTPases, but it also acts as a guanine exchange factor (GEF) toward RagA and RagB. Ragulator senses amino acid availability via the activity of the V-ATPase and via the interaction with a newly discovered lysosomal amino acid transporter, SLC38A9.

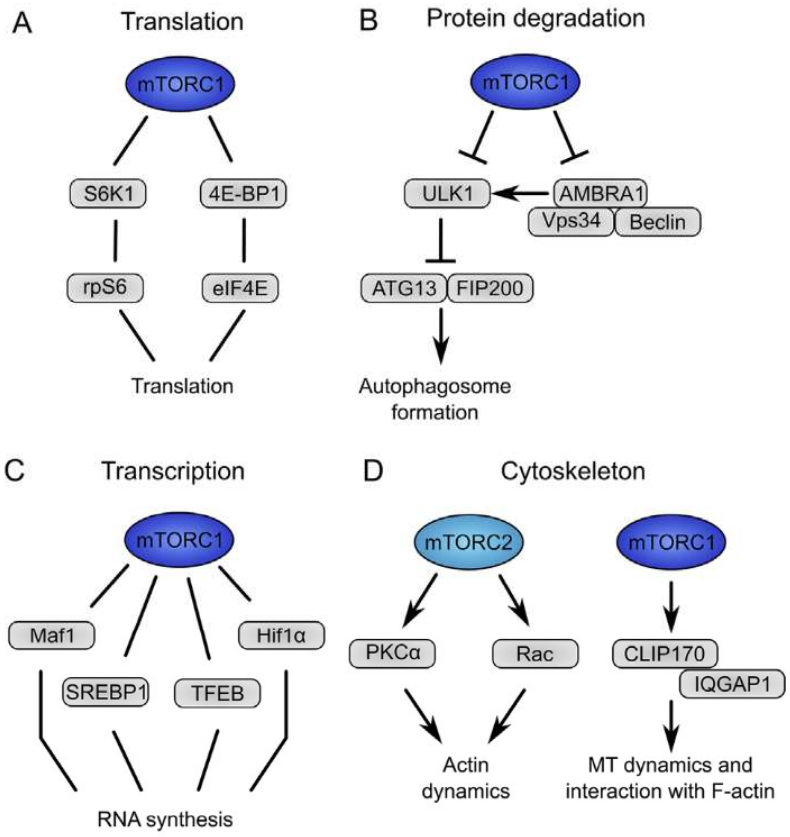


Fig. 3. mTOR targets and downstream cellular processes. (A) Translation. mTORC1 controls translation initiation acting on its best known substrates – 4E-BP1 and S6K1. (B) Autophagy. Under nutrient-rich conditions, mTORC1 interacts via Raptor with the ULK1–Atg13–FIP200 complex. Phosphorylation of ULK1 by mTORC1 prevents initiation of autophagy. When amino acids level is low, mTORC1 is released from the ULK1–Atg13–FIP200 complex and autophagy is promoted. Another way, by which autophagy is controlled by mTOR is the phosphorylation of AMBRA, a part of the Vps34-Beclin1 complex. mTOR-phosphorylated AMBRA is sequestered from the complex that it forms with TRAF6, which weakens the progression of autophagy. (C) Transcription. Several transcription factors (TFs) including MAF1, SREBP1, HIF1α and TFEB were proven to be mTORC1 targets. Phosphorylation by mTOR in some cases regulates cellular distribution of TFs (e.g., TFEB). (D) Cytoskeleton. mTORC1 controls interaction of F-actin and microtubules regulating interaction of its substrate CLIP-170 with an actin-binding protein IQGAP1. mTORC2 controls F-actin dynamics via PKCα and small GTPAse Rac1.

Resources

https://jonlieffmd.com/blog/intelligent-protein-mtor

LU 4.7 Imprinted brain theory from a neurobiological perspective

Introduction

The aim of this meeting is two-fold. First we will discuss the role of mTOR in neuroplasticity and collect evidence for the role of the mTOR pathway in ASD and PSD. During the second part of the meeting, we will summarize all the neurobiological evidence we gathered during this week's meeting related to the imprinted brain theory.

Literature

- Winden KD, Ebrahimi-Fakhari D & Sahin M. Abnormal mTOR activation autism. Annu. Rev. Neurosci 2018. 41:1-23; https://doi.org/10.1146/annurev- neuro-080317- 061747
- Howell KR, Law AJ. Neurodevelopmental concepts of schizophrenia in the genome-wide association era: AKT/mTOR signaling as a pathological mediator of genetic and environmental programming during development. Schizophrenia Research 2020. 217:95-104; https://doi.org/10.1016/j.schres.2019.08.036

Part I: mTOR pathway in ASD and PSD (60 minutes).

Assignment 1

Shortly discuss the mTOR pathway and it's role in neuronal plasticity. Make sure everyone in the peer-group understands before you continu with the next assignments.

Assignment 2

Badcock & Crespi do not explicitily discuss the mTOR pathway in their paper, but they do refer to one of it's regulators, namely the PI3K pathway. Explain the regulatory effect of the PI3K pathway on mTOR activity.

Assignment 3

Below you find a schematic overview of inter-relationship between mTOR pathway, neural plasticity and autism and schizophrenia, as proposed by Crespi (2019). In this assignment you will compare the evidence presented in this scheme to evidence presented in two review papers that selectively reviewed the involvement of the mTOR pathway in either autism or schizophrenia (see resources below).

Instruction:

As a group, divide tasks: 3-4 people look for the evidence on autism and 3-4 people look for the evidence on schizophrenia. The most important section(s) of each review paper are highlighted. Complement the scheme by adding evidence from the review papers.

- Does the evidence from the review paper support or oppose Crespi's hypothesis on the role of mTOR signaling in autism and schizophrenia?
- Is the evidence in line with the general hypothesis concertning changes in neuroplasticity in autism and schizophrenia, as proposed in Forrest et al 2018 (meeting 6)?

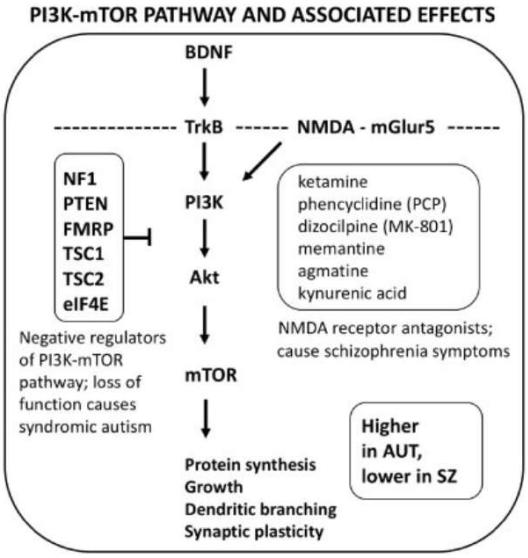


Figure 2. Highly simplified depiction of the inter-relationships of the BDNF-TrkB, NMDA-mGLur5, and PI3K- mTOR systems, that impact upon pathways highly relevant to autism and psychotic-affective conditions. Arrows refer to activation, and the blunt tip refers to negative regulation (reducing activation). NMDA antagonists cause psychological and physiological shifts in the direction of the phenotypes of psychosis. Dashed line refers to synaptic cell membrane. See text for details

Crespi 2019. Evolution, Medicine, and Public Health pp. 149–168

PART II: The imprinted brain theory from a neurobiological perspective (30 minutes)

Assignment 4

Gather all the evidence we have reviewed this week on the neurobiological changes seen in autism and schizophrenia in relation to the imprinted brain theory:

1. On what aspects do ASD and PSD differ from each other?
2. To what extent can you argue that these deficits represent to extremes from one continuum? What arguments support, and what arguments oppose, this statement?
3. Summarize the arguments supporting and opposing the statement that the neurobiological changes in ASD and PSD are two ends of the same continuum. Add the most important arguments to the joint summary table (general channel – files section – meeting 7).

General discussion (30 minutes)

Some of you will be asked to discuss their arguments during group discussion. On basis of these arguments we will discuss the current state of evidence in relation to the neurobiological aspects of the imprinted brain theory.

Resources

Howell Law 2020.pdf

Winden et al 2018.pdf

Week 5 Molecular genetics and epigenetics

LU P5.1 Consultation meeting - literature research

Preparation consultation meeting

- Prepare an overview of the questions that have come up during your literature search and you would like to discuss with your teacher. If you have specific questions about concepts/methods etc discussed within a specific publication, make sure to also include a link to the specific publication. This allows your teacher to adequately prepare for the consultation meeting. **Upload your questions to your MS Teams project group-channel before March 8th, 23:59 hrs**
- Before the meeting, reflect on the following questions about interdisciplinary research:

1.
    1.
        1. What's the most important thing you learned (until now) about doing interdisciplinary research?
        2. What challenges did you face? Can you give an example?
        3. How did you deal with these challenges?

On March 9th, you will have a 20-minutes consultation meeting with your project supervisor. This meeting will be scheduled within the time slot 13:15-15:00 hours. Exact time of your meeting will be announced within your project group-channel.

LU 5.1 Introduction

Molecular genetics is the field of biology that studies the structure and function of genes at a molecular level. The study of chromosomes and gene expression of an organism can give insight into heredity, genetic variation, and mutations, which is useful in understanding and treating genetic diseases. In this part of the module, students will be allowed to refresh their prior knowledge and understanding of molecular genetics. For those students having little background in this area, some easily accessible sources are offered to catch up.

Learning objectives

At the conclusion of this learning activity, you should be able to:

1. explain the central dogma of molecular biology
2. define the structure of DNA/RNA and their building blocks
3. explain the process of DNA replication
4. define the structure of proteins and their building blocks
5. explain the processes of DNA transcription and translation
6. explain how gene expression is regulated

This learning unit contains the following topics:

- DNA structure and replication (LU 5.3)
- Protein synthesis (LU 5.4)
- Regulation of gene expression (LU 5.5)
- Epigenetics (LU 5.6 - 5.8)

Finishing all learning units for this week takes approximately 8 hours (or perhaps more or less, dependent on your background and curiosity).

LU 5.2 DNA from the BEGINNING

If you have little background in molecular biology, you could check out sections 15-17 and 19-24 in **Molecules of genetics** on the website of DNA from the BEGINNING. For a quick orientation use the tab ***Concept***, for a bit more fun and extensive explanations use ***Animation***.

Link to the website DNA from the BEGINNING

If you already have ample background in molecular biology, you could skip this learning unit for now and come back here later and have some fun with DNA from the BEGINNING.

LU 5.3 DNA structure and replication

DNA, or deoxyribonucleic acid, is a long molecule that contains our unique genetic code. Like a recipe book it holds the instructions for making all the proteins in our bodies. Almost every cell in our body contains DNA. When cells divide, the DNA should be copied in order for each cell to have its own package of DNA. This process is called DNA replication.

For this learning activity, please view this 12:58 min video. It goes without saying that making notes while viewing videos is a clever thing to do.

https://www.youtube.com/watch?v=8kK2zwjRV0M

If you can't get enough, try this fancy 8:11 min video from 'Amoeba Sisters' Sarina Peterson and Brianna Rapini from Texas.

https://www.youtube.com/watch?v=Qqe4thU-os8

Fascinated? Check out the website of your**genome** (see Resources below) for more exciting stuff.

Resources

https://www.yourgenome.org/

LU 5.3a Check your understanding I

In the following quiz 12 short answer questions are asked that are related to the previous learning activity.

1. Explain why DNA replication can not proceed without the involvement of an RNA primer.
2. What is the function of helicase enzymes?
3. In what step of the DNA replication process is DNA polymerase I involved?
4. Which enzyme produces Okazaki fragments?
5. Hank distinguishes the ‘good guy strand’ and the ‘scumbag strand’ while explaining DNA replication. What does he mean by that, and how do these two strands differ in the process of DNA replication?
6. What keeps two DNA strands together?
7. Make a list of enzymes and their function that are involved in the replication of DNA, and order the respective enzymes according the consecutive steps in the replication process.
8. The human genome contains 3.1 billion base pairs. The replication enzymes can copy at a rate of 50 base pairs per second. At this rate it would take approximately 2 years to copy one DNA molecule. Replication occurs much faster than that. How?
9. What specific property of DNA polymerase III is responsible for the fact that the DNA replication process differs for the leading and lagging strands?
10. What would be the result if a mutation in the gene coding for the enzyme gyrase would result in a non-functional gyrase enzyme?
11. Ciprofloxacin, a fluoroquinolone antibiotic that fights bacteria in the body, is a gyrase inhibitor. Please explain why only bacteria are affected by this drug, but not human cells.
12. What does it mean that DNA polymerases can proofread?

LU 5.3b Check your understanding II

Use this quiz with 10 multiple choice questions to check your knowledge and understanding.
Your results are not recorded and do not play any role in the grading in this module.

Q1 DNA replication is

a. Conservative
b. Non-conservative
c. Semi-conservative
d. None of the above

Q2 Which of the following is true about DNA polymerase?

a. It can synthesize DNA in the 5’ to 3’ direction
b. It can synthesize DNA in the 3’ to 5’ direction
c. It can synthesize mRNA in the 3’ to 5’ direction
d. It can synthesize mRNA in the 5’ to 3’ direction

Q3 A template strand of DNA is 3' TAGGCATTGCA 5'.
What is the complementary DNA strand that is created from this template during replication?

a. 5' ATCCGTAACGT 3'
b. 5' AUCCGUAACGU 3'
c. 5' TAGGCATTGCA 3'
d. 5' TGCAATGCCTA 3'

Q4 DNA synthesis is

a. unidirectional
b. bidirectional
c. nondirectional
d. multidirectional

Q5 Specific chromosomal locations from where replication begins are called

a. points of interest
b. origins of replication
c. loci
d. chromosomal arms

Q6 Most of mistakes during DNA replication are corrected by

a. DNA ligase
b. gyrase
c. DNA polymerase
d. Helicase

Q7 A single base substitution is called

a. frameshift mutation
b. repeat expansion
c. point mutation
d. recombination

Q8 In terms of DNA and RNA structure, what is a nucleotide?

a. A nucleotide is a heterocyclic base
b. A nucleotide is a sugar molecule covalently bound to a heterocyclic base
c. A nucleotide is a sugar molecule bound to phosphate groups and a heterocyclic base
d. A nucleotide is a heterocyclic base bound to phosphate groups

Q9 DNA exists in a double stranded form whereas RNA is mainly a single stranded molecule. What is the likely reason for DNA being double stranded?

a. RNA strands cannot form base pairs
b. Double stranded DNA is a more stable structure
c. DNA cannot exist in the single stranded form
d. It is easier to replicate double stranded DNA than single stranded DNA

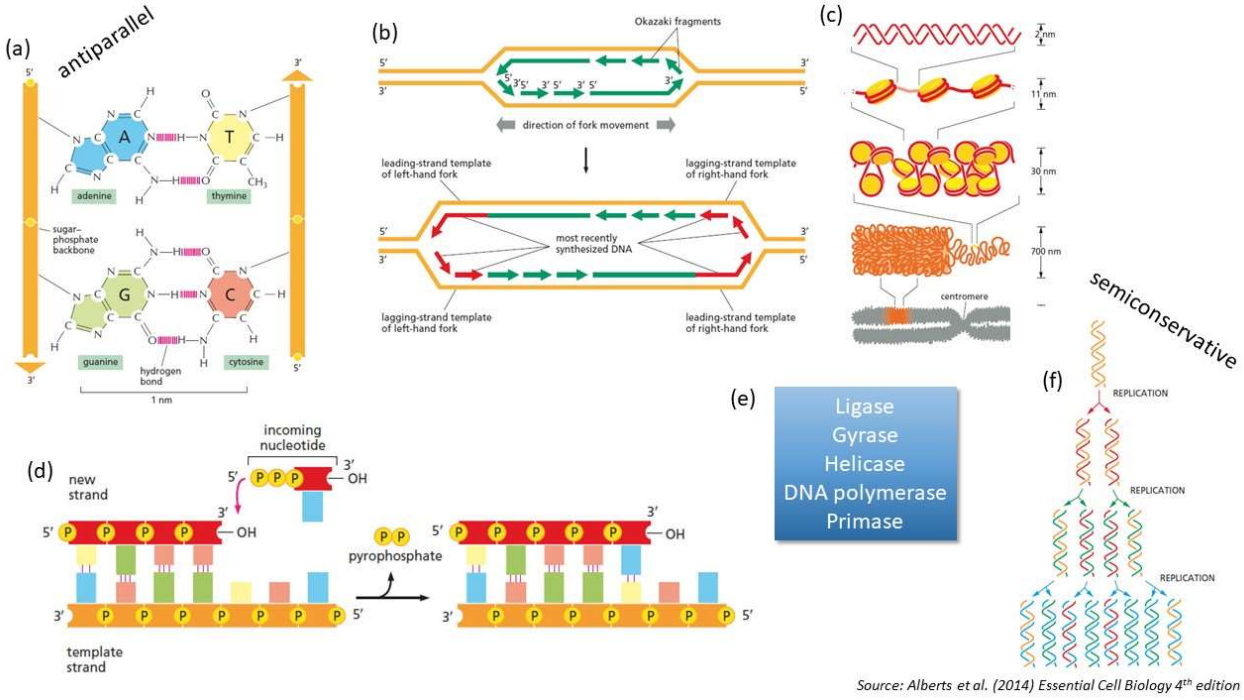
Q10 Which of the following statements is true of DNA damage?

a. All DNA damage results in diseases such as cancer
b. Most DNA damage is repaired by the cell
c. All DNA damage is caused by physical, chemical or biological agents
d. Most DNA damage is advantageous to the cell

LU 5.3c Check your understanding III

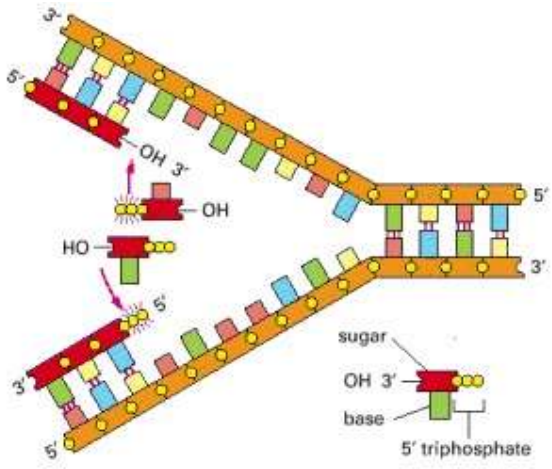
Below you see some piccies dealing with aspects of DNA replication. For every figure a - f write a **full explanation** of what is shown. Keep your notes handy at our next meeting (LU 5.9). You will then give and receive feedback to/from your group members.

Right click on the figure and choose 'open image in new tab' to view a larger version of the figure.



Source: Alberts et al. (2014) Essential Cell Biology 4th edition

LU 5.3d Some advanced problems



Q1 This is an incorrect model of DNA replication. What is wrong, and why?

Q2 Suppose that DNA polymerases would be able to extend existing nucleotide chains from the 3′ as well as the 5′ end. This would then lead to newly synthesized DNA chains with many faulty nucleotides. Please give an explanation for this. Use a figure to illustrate your answer.

Please write down your answers and bring them to the next class meeting (LU 5.9).

Want to read about DNA replication in more depth? Just for fun? Have a look at the resource below.

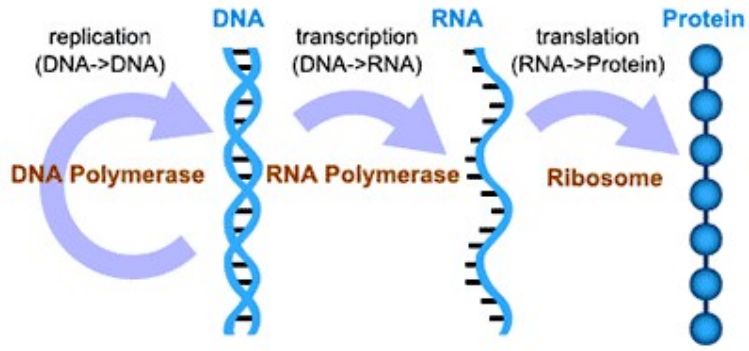
Resources

https://www.ncbi.nlm.nih.gov/books/NBK26850/

LU 5.4 Protein synthesis

Proteins are the "workhorse" molecules of life, taking part in essentially every structure and activity of life. They are building materials for living cells, appearing in the structures inside the cell and within the cell membrane. They carry oxygen, they build tissue, they copy DNA for the next generation - they do all the work in any organism.

Proteins are synthesized through the joint action of DNA, RNA, and .... proteins. The global picture is displayed in the figure below, which is also named the central dogma of molecular biology, or even the central dogma of life.



Watch this 8:46 min video from the 'Amoeba Sisters' to learn about the process of protein synthesis.

https://youtu.be/oefAI2x2CQM

In the next module you can check your understanding.

LU 5.4a Check your understanding

Use this quiz with 11 multiple choice questions to check your knowledge and understanding.
Your results are not recorded and do not play any role in the grading in this course.

Q1 What amino acid is represented by the codon UUA? Use an RNA codon table (there are plenty on the internet).

a. phenylalanine
b. leucine
c. tyrosine
d. stop codon

Q2 The process of making an mRNA strand from a DNA template is called

a. replication
b. translation
c. transcription
d. elongation

Q3 Translation takes place in the

a. mitochondria
b. nucleus
c. chloroplast
d. cytoplasm

Q4 Contains the bases adenine, uracil, cytosine and guanine

a. DNA
b. RNA
c. both DNA and RNA
d. neither DNA nor RNA

Q5 Ribose is the sugar present in the nucleotides of

a. DNA
b. RNA
c. both DNA and RNA
d. neither DNA nor RNA

Q6 This molecule brings amino acids to the ribosome

a. mRNA
b. tRNA
c. rRNA
d. DNA

Q7 What type of mutation is represented in the second strand of DNA?

TACGGCACT
TACGGACT

a. insertion
b. substitution
c. deletion
d. no mutation

Q8 This molecule carries the genetic code to the ribosome

a. mRNA
b. rRNA
c. tRNA
d. DNA

Q9 The process of using an mRNA to make a protein is called

a. replication
b. elongation
c. transcription
d. translation

Q10 Transcription takes place in the

a. nucleus
b. cytosol
c. mitochondria
d. Golgi apparatus

Q11 This molecule cannot leave the nucleus

a. DNA
b. RNA
c. transcription factor

LU 5.4b Find the finest animation on the web

The internet is a rich source for movies, animations, etc. that explain the process of protein synthesis.
You are challenged to browse the internet to try and find THE BEST ANIMATION of protein synthesis.
Post the URL in our team 'The imprinted brain 2021', in the channel 'Interesting stuff', to share it with your fellow students. Also briefly explain why you think this is a useful animation.

Reward? The finest animation will be used in next year's module.

LU 5.5 Regulation of gene expression

For a cell to function properly, necessary proteins must be synthesized at the proper time. All cells control or regulate the synthesis of proteins from information encoded in their DNA. The process of turning on a gene to produce RNA and protein is called **gene expression**. Whether in a simple unicellular organism or a complex multi-cellular organism, each cell controls when and how its genes are expressed. For this to occur, there must be a mechanism to control when a gene is expressed to make RNA and protein, how much of the protein is made, and when it is time to stop making that protein because it is no longer needed. Gene expression is primarily controlled at the level of transcription, largely as a result of binding of proteins to specific sites on DNA.

Allow professor Dave to explain the regulation of gene expression (13.06 min).

https://youtu.be/J9jhg90A7Lw

OK, now it's time to **read** about the regulation of gene expression. Please study gene regulation as explained by the Khan Academy (see link below). Reading directions: How can the cellular proteome be regulated before, during, and after transcription and translation?

You may use concepts 8.1 - 8.3 in chapter 8 from Campbell Biology for reference (see resources below).

Resources

Reece - Campbell Biology 10th ed (2014) Ch18.pdf

https://www.khanacademy.org/science/biology/gene-regulation/gene-regulation-in-eukaryotes/a/overview

LU 5.5a Check your understanding

Please answer the following questions, and bring your written answers to our next class meeting for feedback.

Q1

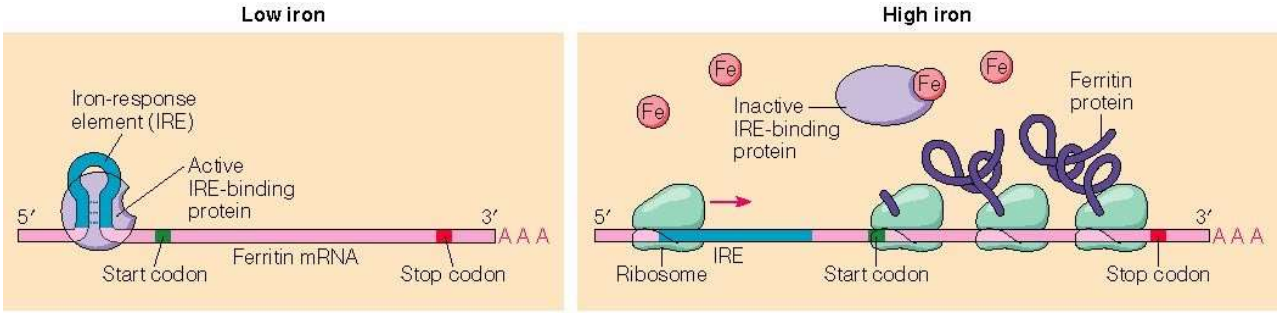
Please explain the concept of 'differential gene expression'. What is the effect of differential gene expression in the body?

Q2

When an RNA transcript is first made in a eukaryotic cell, it is considered a **pre-mRNA** and must be processed into a **messenger RNA** (**mRNA)**.
Pre-mRNA processing involves splicing, alternative splicing, adding a 5' cap, and a 3' poly-A tail. Explain in your own words what the respective functions are of these changes to pre-mRNA.

Q3

Ferritin is a universal intracellular protein that stores iron and releases it in a controlled fashion. If iron concentrations in the body increase, cells will produce more ferritin. The figure below shows how iron regulates the synthesis of ferritin.



Please describe in detail what is displayed in this figure and explain how iron regulates ferritin synthesis.
Right click on the figure and choose 'open image in new tab' to view a larger version of the figure.

Q4a

Science student Tim wants to activate the transcription of gene A to make mRNA. He therefore makes a transcription factor himself. This transcription factor consists of a transcription activating domain and a DNA binding domain. This DNA binding domain consists of six zinc fingers that recognize and bind to a specific sequence in the promoter of gene A. Tim is going to test the transcription factor in a test tube, which also contains all the necessary components for basic transcription. The self-made transcription factor indeed appears to activate transcription of gene A.

List all components that must be present in addition to the self-made transcription factor to enable transcription of gene A.

Q4b

Tim then manages that the self-made transcription factor is actually expressed in cells. Although it is clear that the cell generates this transcription factor, and that it is not broken down by the cell, there is no transcription of gene A. Further investigation revealed that the DNA of gene A is not mutated.

Give TWO possible explanations for the fact that the self-made transcription factor can activate the transcription of gene A in a test tube, but not in the cells.

LU 5.6 Introduction to epigenetics

Epigenetics is the study of heritable changes in gene expression (active versus inactive genes) that do not involve changes to the underlying DNA sequence — a change in phenotype without a change in genotype — which in turn affects how cells read the genes.

The very short video below (1:47 min) tells you a little bit more about the epigenome.

https://vimeo.com/42578320

And here is some more elaborate and entertaining talk about epigenetics (52:03 min).

https://youtu.be/-exzIPGKxME

Optional reading: You may have a look at (one or more of) the resources below to learn more about epigenetics.

Resources

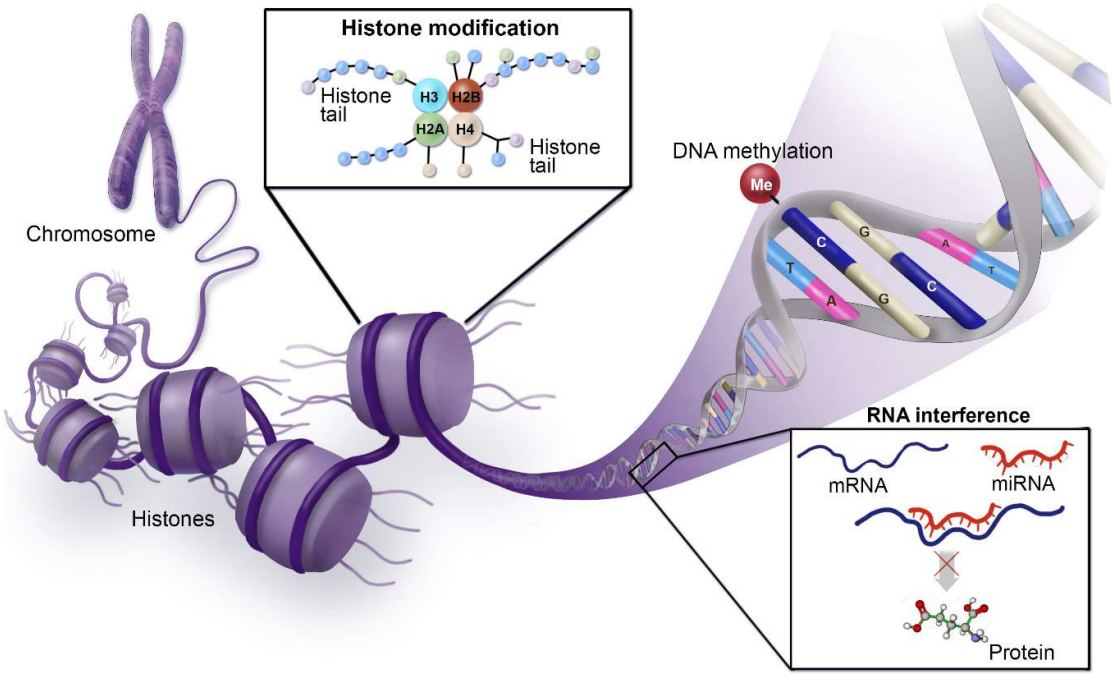
https://learn.genetics.utah.edu/content/epigenetics/

https://bscb.org/learning-resources/softcell-e-learning/epigenetics-its-not-just-genes-that-make-us/

LU 5.7 Molecular mechanisms of epigenetics

Epigenetic programming includes a variety of reversible (but heritable) modifications to the genome that switch genes on and off. These mechanisms include:

1. DNA methylation and hydroxymethylation
2. Histone modifications
3. Chromatin remodeling
4. MicroRNAs



Taken from: https://www.hematology.org/Research/Recommendations/Research-Agenda/3821.aspx

In the video lecture below, dr. Ian Wood explains epigenetic marks (24:48 min).

Private link

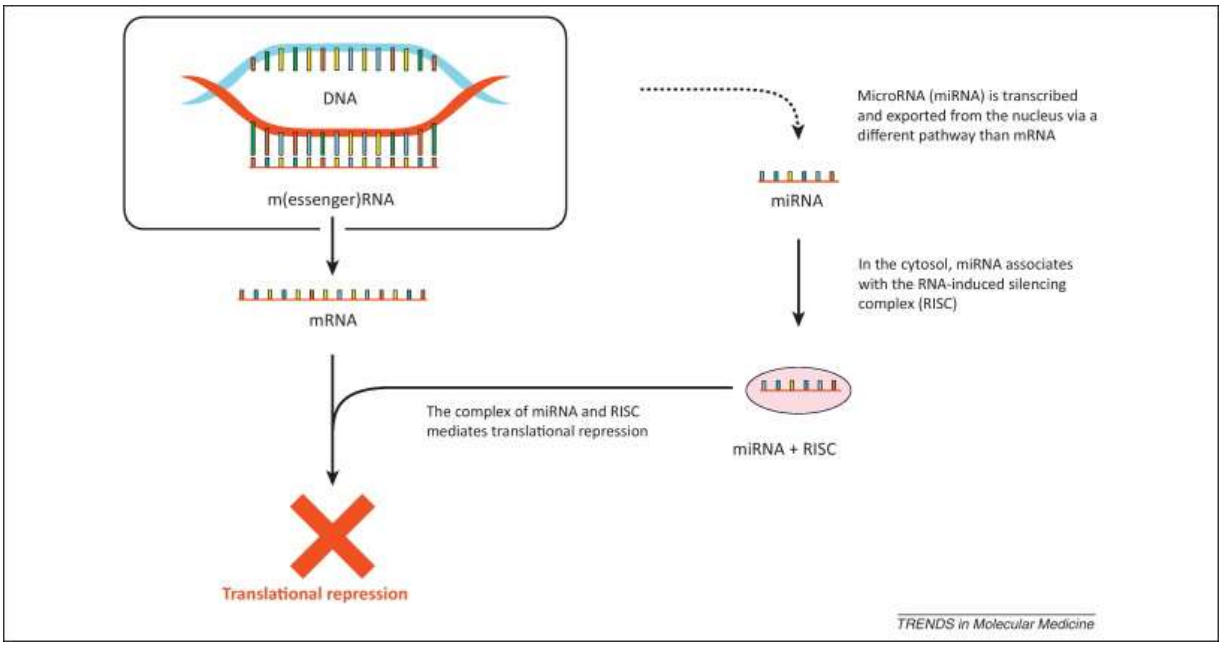
Optional reading: the molecular mechanisms of epigenetics are explained in depth in papers by Tammen et al. (2013) -- first link, and by Fessele et al. (2018) -- second link.

Resources

Epigenetic marks.pptx
https://doi.org/10.1016/j.mam.2012.07.018
https://doi.org/10.1177/1099800417742967

LU 5.8 Focus on microRNAs in epigenetic regulation

MicroRNAs (miRNAs) are small noncoding RNAs, approximately 18–25 nucleotides in length, now recognized as one of the major regulatory gene families in eukaryotes. Recent advances have been made in understanding the complicated roles of miRNAs in epigenetic regulation. The figure below gives a schematic overview of the function of miRNAs.



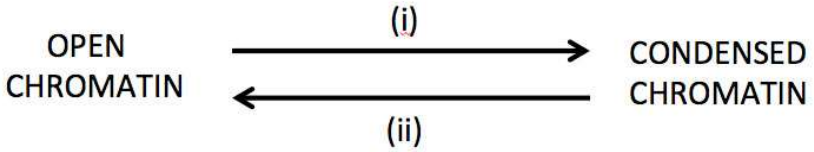
Now read the paper by Yao et al. (2019), and while reading make a concept map of the reciprocal actions of miRNA and epigenetic pathway. Don't lose yourself in all the details, try to abstract the bigger picture.

Please bring your concept map to our next class meeting (what else?).

LU 5.8a Check your understanding

In the following quiz 6 short answer questions are asked that are related to the previous learning activity.

1. Define the term epigenetics.
2. Describe the physical state of the genome when genes are inactive vs. when genes are active.
3. Often, the physical characteristics of genetically identical twins become increasingly different as they age, even at the molecular level. Explain why this is so.
4. Name 3-4 environmental factors that influence the epigenome.
5. With respect to the interconversion between open and condensed chromatin shown below:



Which of the directions (i) or (ii) would you anticipate would be the consequence of the following types of chromatin modification?

a) Histone acetylation.
b) DNA methylation.
c) Histone methylation.
d) Histone deacetylation.
e) DNA demethylation.

Please explain your answer(s).

6. With respect to microRNAs, which, if any, of the following statements, is false?

a) MicroRNA is a generic term that covers all tiny RNAs, ones that are less than 35 nucleotides long when mature.
b) MicroRNAs usually work as transcription factors.
c) MicroRNAs regulate target genes by binding to complementary sequences on one DNA strand of the target gene.
d) MicroRNAs normally regulate the expression of just a single target gene.

Please explain your answer(s).

LU 5.9 Meeting: Discuss (epi)genetic mechanisms

This week you learned a lot about molecular genetics and epigenetics in general, as a stepping stone to the topic of genetic imprinting (week 6) and the role in Badcock's and Crespi's theory (week 7).

Today you will have time to reflect on what you learned, and what you don't understand yet. Please bring all your notes, concept maps, questions etc. to today's meeting (pay particular attention to LU 5.3c / 5.3d / 5.5a / 5.8 in your preparation for today).

Week 6 Genetic imprinting

LU P6.1 consultation meeting - literature research

Preparation consultation meeting

- Prepare an overview of the questions that have come up during your literature search and you would like to discuss with your teacher. If you have specific questions about concepts/methods etc discussed within a specific publication, make sure to also include a link to the specific publication. This allows your teacher to adequately prepare for the consultation meeting. **Upload your questions to your MS Teams project group-channel before March 15th, 23:59 hrs**

- Before the meeting, reflect on the following questions:
    - About interdisciplinary research:
        - What's the most important thing you learned (until now) about doing interdisciplinary research?
        - What challenges did you face? Can you give an example?
        - How did you deal with these challenges?
    - About teamwork:
        - What's the most important thing you learned about working in an interdisciplinary team? Why do you think so?
        - To what extent do you experience added value of working on your project within an interdisciplinary team? And why?
        - What challenges did you face until now? Can you give an example?
        - How did you deal with these challenges? Were you satisfied with the result? (Why?)
        - What are your learning goals for the next weeks.

On March 16th, you will have a 20-minutes consultation meeting with your project supervisor. This meeting will be scheduled within the time slot 13:15-15:00 hours. Exact time of your meeting will be announced within your project group-channel.

LU 6.1 Introduction

In genetic (or genomic) imprinting the ability of a gene to be expressed depends upon the sex of the parent who passed on the gene. In some cases imprinted genes are expressed when the are inherited from the mother. in other cases they are expressed when inherited from the father. Unlike genomic mutations that can affect the ability of inherited genes to be expressed, genomic imprinting does not affect the DNA sequence itself. Genomic imprinting affects gene expression by chemically modifying DNA and/or altering the chromatin structure. Often, genomic imprinting results in a gene being expressed only in the chromosome inherited from one or the other parent. While this is a normal process, when combined with genomic mutations, disease can result. For example, Prader-Willi syndrome and Angelman syndrome are two distinct diseases caused by a deletion in the same part of chromosome 15. When this deletion occurs on the chromosome 15 that came from the father, the child will have Prader-Willi syndrome. However, when the deletion occurs on the chromosome 15 that came from the mother, the child will develop Angelman syndrome. This occurs because genes located in this region undergo genomic imprinting.

Here is a short, stylised and gentle introduction

https://www.youtube.com/watch?v=WIH68Ppnj_w

This video provides an overview of some of the concepts of imprinting:

https://www.youtube.com/watch?v=RGoAX_4QW1U

Some links to further introductory resources:

https://learn.genetics.utah.edu/content/epigenetics/imprinting/

https://bscb.org/learning-resources/softcell-e-learning/epigenetics-its-not-just-genes-that-make-us/

LU 6.2 What should I learn?

To try and give you some focus around the topic of imprinting here are the learning outcomes you should aim to achieve from work within this unit.

- Understand and be able to explain what imprinting is, when it occurs and what the result is.

- Explain and discuss the theories on why imprinting exists.

- Be able to give examples of disorders that involve the brain and are known/or thought to involve errors in imprinting.

- Describe how Prader-Willi and Angelman syndromes are caused (and maybe some other examples but PW/AS is the best).

- Be able to consider how imprinting of specific genes could influence the brain and behaviour and provide some example candidate genes.

LU 6.3 What do we know about imprinting?

Here is a brief textbook introduction to imprinting with a very clear pictorial representation of the imprinting:

Link : Genomic Imprinting Requires DNA Methylation

The following review is written by Wolf Reik, who works in Cambridge and is an expert on imprinting.

Link: Genomic imprinting: parental influence on the genome. Wolf Reik and Jorn Walter, *Nature Reviews Genetics* volume 2, pages 21–32(2001)

LU 6.4 Check your understanding

Check you are able to answer these questions and provide short explanations for these concepts

1. What is genomic imprinting?
2. Why is imprinting thought to occur?
3. Explain the difference between monoallelic expression and parental-specific allelic bias
4. What is kinship theory of imprinting?
5. Draw a genetic inheritance diagram of a pair of chromosomes and indicating the inheritance of a gene on the chromosome that is paternally imprinted. The diagram should show the chromosome in the parents and all different combinations possible in the offspring. Indicate the imprint with an asterisk.
   How would your diagram change if the gene was maternally inherited?

LU 6.5 Self and Group study assignment - Syndromes associated with imprinting

This review covers some of the material as the one written by Reik but (in my opinion) a bit easier to read in places and has more detail on human disorders associated with imprinting

https://www.sciencedirect.com/science/article/pii/S0098299712000817?via%3Dihub

In your groups within the meeting you will be given 30 minutes to prepare a 5 minute (max) presentation that provides explanation of the imprinting disorders below. Pay particular attention to features that might impact on the brain and/or relevant to Autism and Psychosis. To prepare you should individually put together what you think should be included - try to keep to a single Powerpoint page and have at least one diagram. Below are the group assignments and a starting place for you to look for relevant information.

Groups 2 and 6: Silver Russell Syndrome - https://omim.org/entry/180860

Groups 3 and 4: Prader-Willi Syndrome - https://omim.org/entry/176270

Groups 5 and 1: Angelman Syndrome - https://omim.org/entry/105830

Group 7: Beckwith-Wiedemann Syndrome - https://omim.org/entry/130650

Below is a short video explaining the changes that could account for Prader-Willi and Angelman syndromes. Notice how diagrams are used to help with the explanation and that only a subset of facts/features are included which are those that the creator thought important. You should consider how you would represent the information you want to include but in a static form.

https://youtu.be/nYvm4Rsh7t8

LU 6.6 Imprinting disorders

In this meeting:

1) We will check a general understanding of imprinting

2) You will work in your groups to put together a presentation of the disorder given to your group

3) Groups will present on their given disorder (5 min max)

4) We will consider how what we have learnt this week fits in with the bigger picture

5) Look forward to week 7

Week 7 The imprinted brain theory

LU 7.1 Introduction

Badcock & Crespi used different disciplinary perspectives to come up with their Imprinted Brain Theory. You have studied these disciplines in recent weeks. You already came across literature data that support the Imprinted Brain Theory, but also found information that contradicts the theory.

Now is the time to weigh the pros and cons. This week you will review and integrate all the information you have gathered, perhaps find new information, and make an overview.

Assignment
Uneven groups 1, 3, 5, and 7 make an overview of arguments that support the Imprinted Brain Theory.
Even groups 2, 4, and 6 make an overview of arguments that contradict the theory.

All groups make a PowerPoint presentation (max 3 slides). It should contain your arguments, figures and tables to illustrate the arguments, and literature references that support your arguments.

The meeting on Tuesday (LU 7.2) can be used for sharing and discussing all arguments and to make the PowerPoint presentation.

You will use the PowerPoint presentation on Thursday (LU 7.3) to 'convince' others.

LU 7.2 Pros and cons of the Imprinted Brain Theory

In today's meeting you will work in your peer tutoring group to collect and discuss all information that either supports the Imprinted Brain Theory (uneven groups) or contradict it (even groups). You will make a PowerPoint presentation that can be used for the 'battle' (see LU 7.3).

LU 7.3 The battle

Today you will try and convince your opponents. The arenas are setup as separate channels in Teams, as follows:

Arena A - Groups 1 and 2
Arena B - Groups 3 and 4
Arena C - Groups 5, 6, and 7

Groups will present (and explain) their arguments, and discuss the final outcome: do we have enough evidence that the Imprinted Brain Theory holds true? Or should we reject the theory? Or....?

In the concluding plenary part of the meeting the 3 arenas shortly present their conclusions.

Week 8 Self-study and exam

Exam

Written exam - more information will be / has been made available via BlackBoard and E-mail announcements.

Week 9 Integration phase interdisciplinary project

LU P9.1 disciplinary grounding

Introduction

The final step of phase 1 in the interdisciplinary research process is to exchange the disciplinary findings within your project group. To this end, every project group member will **prepare a short, informal presentation** (5 minutes) in which you discuss the most important insights from your discipline and the scientific theories and experimental findings that support those insights. When phase 1 is concluded, you can continue with phase 2, i.e. perspective taking. The aim of this phase is to acknowledge the different perspectives and identify common ground.

Assignment (45 min)

Each project member presents his/her findings. During each presentation the other project members are asked to write down notes focused on results, and contrasts. After every presentation you discuss the results and write down the remaining questions.

LU P9.1 Perspective taking & Creating common ground

Perspective taking

This step is the first integrative step. Conflicting views or just differences may occur at the level of (1) insights, (2) concepts, (3) assumptions and (4) theories.

In case of differences these are the relevant questions (see your data-management file):

- Which perspectives are offered?
- Which assumptions are used?
- Which theories are used?
- What counts as evidence?
- Which concepts and terminologies are used to describe the problem?

Note: Different disciplines sometimes use the same terminology or concept to indicate different phenomena or the other way around. Make sure that you understand each other well enough within your team to avoid confusion or misconceptions which would prevent your ability to switch from one perspective to another.

There are three possible outcomes to this process:

- There is no true conflict between insights, but the similarity is hidden by terminology or bias
- Insights are different but not contradictory; they present alternatives
- Insights exclude each other

Assignment 1: Identifying conflicts or differences, similarities (40 min)

List the outcome of the discussions (results/insights, contrasts from previous meeting) in a digital file and share this within your teams project groupchannel. Take also your management table.

Write down your research question in the middle of a 'whiteboard' (e.g. use a note-function in MS Teams, like freehand) and share this tool so everyone can see it and work in it.

Start a brainstorm session:

In what way do the disciplinary insights contradict or differ from each other?

Conflicting views or just differences may occur at the level of (1) insights, (2) concepts, (3) assumptions and (4) theories.

In case of differences these are the relevant questions (see also your data-management file):

- Which perspectives are offered?
- Which assumptions are used?
- Which theories are used?
- What counts as evidence?
- Which concepts and terminologies are used to describe the problem?
- If disciplines use the same concept: how are the concepts defined and measured?

Visualise your findings in a concept map.

Creating common ground

So far you have mostly been working in a descriptive and evaluative way. You have identified differences between insights, concepts, assumptions, and theories of the most relevant disciplines for your topic. The creative process starts by creating common ground, i.e. the second step of perspective taking. That is, you start looking for ways to reconcile different insights. Sometimes it is possible to discover common ground, finding some sort of common denominator behind differences. But often it needs to be created by setting differences aside and focusing on similarities. (Europe has a long history of wars between nations, but a shared future).

When creating common ground, we identify what different disciplinary insights (concepts, assumptions and theories) have in common. Often, we will see that different disciplines focus on difference aspects of the same issue. In the process of creating common ground, preferences for one or the other should be avoided. Creating common ground starts by attributing equal values to different perspectives. It is not about declaring a winner, but about developing a new, more comprehensive view.

Assignment (30 minutes)

Sit together with your project group in your subchannel. Take your shared document of the DMT, your concept map and your research question.

Discuss the following questions:

· Do you see connection/overlap between the different insights and perspectives?

· Which insights are most relevant for answering your research question?

· Do some insights support each other?

Formulate a preliminary answer to your research question.

LU P9.2 Formulate integrated conclusions

Introduction

The final step in the interdisciplinary research process is the integration of insights on basis of common ground into a more comprehensive understanding. Show how the combination of different theories and methodologies leads to a better explanation or solution. Within your interdisciplinary paper you could try to elaborate on this (difficult) step to trigger innovation.

But first, you will discuss you project with members of other project groups, who have worked on a different topic. This will expose possible unclarities in your preliminary conclusions and underlying evidence and provide feedback you can incorporate when drawing your final conclusions.

Assignment 1 (45 minutes)

The teacher will form new subchannels in Teams (ASD - PSD groups) in which you explain the research question and preliminary answer from your project group to your fellow students and discuss possible unclarities and remaining issues. Make notes because you have to share your findings within your project group.

Assignment 2 (30 minutes)

Discuss in your ASD-PSD group how all your findings relate to Badcock's Imprinted brain theory.

Assignment 3 (30 minutes)

Sit together again with your project group for the wrap up and discuss findings and issues coming from the disciplinary groups and how this affects the interpretation of disciplinary literature and the integrative answer your have formulated to your research question.

Next week, you will present the most important results of your research by means of a short pitch (5 minute presentation) in MS teams.

Week 10 Finalize interdisciplinary project

Project pitches

The session will take place on Thursday April 15th, 13:15 - 15:30 hrs, in MS Teams.

Instructions
The pitches should highlight the research question, main disciplinary results and integrated conclusion of your project.

During the meeting you will pitch your project in 5 minutes, using PowerPoint

Afterwards there is 5-10 minutes available for questions from fellow students and teachers.

All pitches (PowerPoint files) should be handed in at the end of the poster session.