School of Behavioral and Cognitive Neurosciences

February 1, 2024

BCN Winter Meeting

Poster Presentations PhD-students / ReMa-students

Programme

09:00 – 09:30 Registration with coffee
09:30 – 09:40 Welcome by *Wander Lowie*
09:40 – 10:10 BCN board
10:10 – 10:25 Sanne Moorman (FSE)
Illuminating a birdsong model for human speech acquisition and vocal motor control
10:25 – 10:55 Coffee break
10:55 – 11:10 Hakan Karsilar (GMW)
Illusions of Time: Clockwork in the Mind's Eye
11:10 – 11.25 Dörte de Kok (FL)
AppScaling tests for language disorders
11:25 – 11:40 Markus Eronen (FW)
Reduction and complexity in cognitive neuroscience
11:40 – 11.55 Ellie Harding (FMW)
Can you hear me now? Clinical applications to the study of language and music cognition
11:55 – 12:00 PhD council
12:00 – 12:55 Lunch break
12:55 – 13:00 Gathering groups
13:00 – 14:00 Poster group session
14:00 – 14:35 Coffee/tea break + free poster session
14:35 – 14:50 Lecture BCN Dissertation Award winner
14:50 – 15:50 BCN key-note lecture: Makiko Sadataka
When Speech Sounds Become Music: The Curious Effects of Repetition
15:50 – 16:00 Presentation BCN Poster Awards
16:00 – 16:20 BCN Seed Grants
16:20 – 17:00 Drinks

Location:
Marie-Lokezaal, Harmony Building, Oude Kijk in ‘t Jatstraat 26, Groningen

Index (numbers refer to the poster- and page numbers)

Poster Groups PhD-students

Group 1 (gathering at board no. 1)
1 Marit Hidding
2 Lotte Piekema
3 Janine Rook
4 Ivo Meins

Group 2 (gathering at board no. 5)
5 Franciska de Beer
6 Henning Schulte
7 Michael van Dijk
8 Alke Haarsma-Wisselink

Group 3 (gathering at board no. 9)
9 Kim Vos
10 Wenrui Deng
11 Freya Gastmann
12 Lisanne Robbemond

Group 4 (gathering at board no. 13)
13 Ekaterina Dagkesamanskaia
14 Lale Gungordu
15 Amber Heegers
16 Sofie Lovdal

Group 5 (gathering at board no. 17)
17 Ningning Zeng
18 Juliana Dean
19 Floor van den Berg
20 Jaroslav Krc

Group 6 (gathering at board no. 21)
21 Sofia Marcolini
22 Maria João Costa Caiado
23 Mirjam Koster
24 Teresa Mitchell García

Group 7 (gathering at board no. 25)
25 Angèle Picco
26 Sophie van Zonneveld
27 Aliene Reinders
28 Marijke Muller

Group 8 (gathering at board no. 29)
29 Nikki Dreijer
30 Mayerli Prado Rivera
31 Danara Vonk

Group 9 (gathering at board no. 32)
32 Esteban Palacios Contreras
33 Dilce Tanriverdi
34 Xiaolin Zhu
35 Junfei Cao

Poster Groups Research Master-students

Posterboard nos. A1 – R1

Group A (Robbert Havekes – evaluator) - *(gathering at board no. A1)*

A1	Thirza Algra
A2	Franceska Bertolini
B1	Michelle Coppes
B2	Hazal Ekin Dolu
C1	Daniel Fleming

Group B (Sanne Moorman - evaluator) - *(gathering at board no. C2)*

C2	Daniel Grech
D1	Berit Haitjema
D2	Mary-Ann van der Linden
E1	Lucie Munoz

Group C (Niki Gervais - evaluator) - *(gathering at board no. E2)*

E2	Remon Nicolai
F1	Giulia Quagliozzi
F2	Franciska Reis
G1	Emke Sijtsma

Group D (Peter Meerlo - evaluator) - *(gathering at board no. G2)*

G2	Sofie Solvang
H1	Arne Stein
H2	Dimitros Tantis-Tapeinos
I1	Mark Trivanović
I2	Malgorzaa Tybuszewska

Group E (Martien Kas - evaluator) - *(gathering at board no. J1)*

J1	Kris Vasse
J2	Nienke van der Veen
K1	Daniek Versloot
K2	Rianne Vogt
L1	Asimenia Voulgaroglou

BCN Keynote lecture

Dr. Makiko Sadakata
Faculty of Humanities
Music Cognition group
University of Amsterdam

When Speech Sounds Become Music: The Curious Effects of Repetition

Makiko Sadakata is a lecturer at the musicology department of the University of Amsterdam. She is one of the core research members at the Music Cognition Group (MCG) at the Institute for Logic, Language and Computation. Her research revolves around the question of what music is to our mind and how it differs from other sounds, such as language and environmental sounds. Makiko Sadakata is a lecturer at the musicology department of the University of Amsterdam. She is one of the core research members at the Music Cognition Group (MCG) at the Institute for Logic, Language and Computation. Her research revolves around the question of what music is to our mind and how it differs from other sounds, such as language and environmental sounds.
https://www.uva.nl/en/profile/s/a/m.sadakata/m.sadakata.html

1

A Single-Session VR Intervention Addressing Self-Compassion and Self-Criticism With and Without Perspective Change: Results of a Randomized Controlled Experiment

Marit Hidding[1], Wim Veling [1], Gerdina H.M. Pijnenborg[2,3], Elisabeth C.D. van der Stouwe [1]

[1] Department of Psychiatry, University of Groningen, University Medical Center Groningen, Groningen; [2] GGZ Drenthe, Department of Psychotic Disorders, Assen; [3] Faculty of Behavioural and Social Sciences, Department of Clinical and Developmental Neuropsychology, University of Groningen, Groningen

Background
Excessive self-criticism is an important transdiagnostic psychological factor. In contrast, self-compassion can contribute to the resilience and recovery of clinical populations, making this an important target for treatment. Virtual Reality (VR) has the potential to improve existing interventions as it allows for personalized roleplays that can be experienced from different perspectives, by using the novel VR technique of perspective change.

Objective
The current study aimed to investigate the effect of a novel single-session VR intervention for improving self-compassion and diminishing self-criticism, and the added value of changing perspectives.

Design/methods
In total, 68 undergraduate students with high levels of self-criticism were randomized to either the perspective change condition or the control condition. Participants played two roleplays in which they had to react compassionately toward a virtual character that expressed the participants' own self-critical thoughts. In the perspective change condition, after each roleplay a perspective change was used to receive one's own compassionate words.

Results
Results showed that self-compassion increased and self-criticism decreased significantly in both conditions. No significant differences were found for negative and positive affect. Furthermore, no differences were found between the conditions. Thus, receiving compassionate words through perspective change had no additional effect.

Conclusion
Expressing compassion to someone with similar self-criticism showed to be sufficient to reduce self-criticism and increase self-compassion.

2

From assistive to inclusive?
A systematic review of the uses and effects of technology to support people with profound intellectual and multiple disabilities

Lotte Piekema[1], dr. Annet ten Brug[1], dr. Aly Waninge[2,3],
and prof. dr. Annette van der Putten[1]

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Background
Quality of life (QoL) of people with profound intellectual and multiple disabilities (PIMD) can be enhanced by the use of technologies. There are various types of technologies to do this. However, their objectives and effects are understudied. A systematic literature review was therefore conducted to explore this topic.

Objective
Create an overview of evidence-based technologies targeting people with PIMD and their objectives and effects. More knowledge may foster positive attitudes, enabling relatives and healthcare professionals to make informed decisions, thus benefiting people with PIMD.

Design/methods
A search of four databases yielded 64 studies. Data were extracted on their general characteristics, methods and sample characteristics as well as the technology types, QoL domains and application within ecological systems. A narrative synthesis was subsequently developed.

Results
Most of the studies applied assistive technology (AT), with fewer studies focusing on mainstream technology (MT), and technology based on universal design (UD) principles. Technology was most frequently deployed at an individual level and within the microsystem.

Conclusion
Technology can enhance the QoL of people with PIMD, especially on self-determination and personal development. There are indications that although MT and UD-based technologies are used in practice, few studies have examined these technologies. Therefore, there is a knowledge gap regarding the kinds of technologies that are used in practice. Additional research into technology use in PIMD in practice is required.

3

Exploring the link between multilingual experiences, genetic risk factors for Alzheimer's Disease and neurocognition in middle-aged adults

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Background
Aging is associated with a decline in cognitive functioning (Ferguson et al., 2021). Successful aging can be seen as the interaction between modifiable lifestyle factors and fixed factors (e.g., genetics). Various lifestyle factors have been found to improve the brain's resilience against (age-related) cognitive decline (i.e., cognitive reserve, CR). Strikingly, multilingualism has been identified as one of these modifiable lifestyle factors, and has been associated with CR and an attenuation of Alzheimer's Disease (AD) symptoms by approximately 4-5 years (e.g., Anderson et al., 2020).

Objective
Research has so far focused predominantly on the younger and older lifespan, but to fully understand how CR builds up as a function of multilingual life experiences, we need a broader lifespan perspective and thus include middle-aged individuals, which are crucially underrepresented in the present literature. Moreover, in addition to modifiable lifestyle factors (e.g., multilingualism), fixed factors (e.g., genetic predisposition) may make individuals more or less susceptible to cognitive impairment in later life (Alzheimer's Association, 2023). To understand the mechanism underlying the contributions of multilingual experiences to CR, and to understand its implication for AD symptom attenuation, we need to explore the role of genetic risk factors for AD in the age group that just precedes later life.

Design/methods
The present project examines how individual multilingual experiences of middle-aged adults (45-65 years-old) affect neurocognitive outcomes, including behavioral performance on cognitive tasks (Stroop Arrows task, Color-Shape switching task) and functional brain activity during rest and on-task (electroencephalography, functional Near-Infrared Spectroscopy). Crucially, we explore how familial risk for AD modulates the effect of multilingual experiences on neurocognition.

Hypotheses/results
In this presentation, we outline the method that forms the basis of the project. In line with previous research, we predict that greater degrees of multilingual engagement (i.e., more frequent language use in different contexts) induce neurocognitive changes and that genetic predisposition for AD modulates neurocognition (e.g., Grundy et al., 2017; Smith et al, 2023).

Conclusion
To the best of our knowledge, this is one of the first multilingualism studies that actively investigates the middle-age lifespan and includes genetic risk factors for AD. In this way, we are not only able to uniquely relate individual multilingual experiences to cognitive performance in middle adulthood, but we can also explore how familial genetic risk factors modulate this association.

4

VR-SOAP - Virtual Reality Treatment for improving SOcial Activities and Participation of young people with psychosis: a pilot & randomized effect study

Ivo Alexander Meins[1,2,3], Elisabeth Christine Dorothée van der Stouwe[1], Dauw Catharina Muijsson-Bouwman[1], Saskia Anne Nijman[1,3,5], Rinesh Baidjnath Misier[4], Wim Veling[1] and Gerdina Hendrika Maria Pijnenborg[2,3]

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Background
Young people with a psychotic disorder have the same social goals as their healthy peers, but their social networks are smaller, they participate less often in leisure activities and are less successful in work and education. Current treatments have only moderate effects on social functioning and often target one specific domain.

Objective
To develop and investigate effectiveness of a virtual reality treatment for social activities and participation (VR-SOAP)

Design/methods
We developed and piloted a modular VR treatment for social functioning and participation. Presently, we are conducting a randomized controlled trial (RCT) to investigate effectiveness.

Results
Both participants and therapists found the therapy acceptable. Participants and therapists found the intervention simple to comprehend, beneficial, and aligned with their values. Participants expressed increased confidence in their social interactions and reported improvements in skills such as initiating conversations and maintaining a positive outlook. No dropouts occurred during the pilot phase.
The RCT is ongoing.

Conclusion
The intervention showed a high degree of acceptability on all seven dimensions of the acceptability framework. VR-SOAP is well tolerable and perceived as effective. Currently the RCT is ongoing to investigate effectiveness.

5

The influence of sex and menopause on antipsychotic serum concentrations

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* Both authors contributed equally

Background
Most antipsychotics used today are prescribed at using a one-size-fits-all approach, based on male-dominated clinical trials. At the same time, women are more likely to report antipsychotic side effects, and side effects in women are predicted by sex differences in drug pharmacokinetics. On average, sex differences in pharmacokinetics, with estrogen playing a significant role, cause the drug to stay longer in the female body. This is hypothesized to lead to higher serum concentrations in women when a one-size-fits-all approach is used. After menopause, estrogen levels remain low, which is hypothesized to affect antipsychotic serum concentrations.

Objective
We sought to explore sex differences in serum concentrations of 8 commonly used antipsychotics, and examined how these sex differences change after the age of 45.

Design/methods
Antipsychotic concentrations of 11052 plasma samples were analyzed, which were drawn between January 2017 and December 2022 in the Netherlands in 5477 unique adult men and women, with a median of 2 samples per person (IQR=3). The dataset consisted of concentrations of olanzapine (n=1910, 41% female), clozapine (n=6410, 32% female), aripiprazole (n=1967, 41% female), and quetiapine (n=764, 62% female). To investigate the effect of sex on antipsychotic serum concentrations, we employed linear mixed-effects models (LMEMs), accounting for age, time, and including a random intercept for participants. Next, we examined the effect of reaching the age of 45 (i.e., mean age of menopause in women), by dividing the samples according to sex and age (< 45 vs. ≥ 45 years), using LMEMs with a random effect for patient and fixed effect for time. When applicable, FDR-corrected post hoc comparisons were employed to compare men <45 with the other groups and to compare women <45 with women ≥ 45.

Results
We found a significant effect of sex on serum concentrations for 4 antipsychotics, with women having on average higher levels of serum concentrations of olanzapine, clozapine, and aripiprazole. Sex/age-group analyses revealed significant effects for clozapine, aripiprazole, and quetiapine. Pairwise post hoc comparisons revealed that that serum concentrations of clozapine were highest in women <45 compared to men, and compared to women ≥ 45. Serum concentrations of aripiprazole were highest in women ≥ 45, as compared to men <45. Conversely, serum concentrations of quetiapine were lower in women <45, women ≥ 45, and men ≥ 45.

Conclusion
In sum, we found pronounced sex differences in serum concentrations, which differ per antipsychotic and may evolve with advancing age. Our findings suggest that the one-size-fits-all approach for prescribing antipsychotics may not serve both sexes equally, and stresses the need for further research into the sex- and hormone-dependent pharmacokinetic mechanisms of antipsychotics.

6

Detecting and delineating visual field defects based on free-viewing in glaucoma

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Background
Standard Automated Perimetry (SAP) is an important method to measure the visual field (VF). While for visually healthy adults it usually provides reliable results, for many patients it is tiring and difficult to perform.

Objective
In a previous simulation study we described a novel way of detecting and delineating simulated visual field defects from gaze tracked movie viewing. Our method compares a viewer's gaze to that of a group of control participants and derives predictions about the presence of VF defects. Based on this approach, we could distinguish between five archetypical simulated VF defects and no defect. The graphical depiction of the defect's shape and location matched the simulated VF defect shapes on a group level. In the present study, we assessed how well this new method is able to detect and delineate real VF defects.

To assess the performance of the method with VF defects, we applied it to data from 20 participants with glaucoma and 20 age-matched controls who each monocularly viewed a series of 1-minute movie clips while their gaze was being tracked.

Results
Results showed that for most controls, our new analysis predicted an intact visual field, whereas defects were found in participants with glaucoma. For the participants with glaucoma, our predicted delineations of their VF defects did not compare well to those produced by SAP.

Conclusion
We conclude that free-viewing gaze behavior can be used towards detecting the presence of a VF defect. The observed discrepancy between our new method's delineation and SAP with real VF defects suggests that participants with glaucoma have learned to adapt their gaze behavior to maximally utilize their remaining visual field. Further work is needed to accurately delineate defects of clinical groups based on free-viewing.

7

Lost connections: establishing the role of the ‘forceps minor’ in social behavior using chemogenetics and wireless EEG in mice

Michael van Dijk, Martien Kas & Robbert Havekes

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Background
Social withdrawal is a shared symptom across various neuropsychiatric disorders such as Autism, Schizophrenia and Major Depressive Disorder and Alzheimer’s disease. Despite its potential impact on the progression of these disorders, the neurobiological foundations that contribute to diminished sociability remain elusive. Recent studies in humans highlight an association between the reduced integrity in the white matter bundle known as the ‘forceps minor’ (i.e. anterior corpus callossum) and social withdrawal, regardless of the specific disorder.

Objective
This project aims to establish the causal relationship between the forceps minor social withdrawal by experimentally manipulating the activity of this bundle in mice.

Design/methods
Mice will undergo chemogenetic inhibition of the forceps minor, targeting neurons with interhemispheric projections. Automated assessments in a group setting using RFID-assisted social colony setups will measure resulting social behavioral changes. In addition, standard social behavioral assays, such as the 'Three Chamber Sociability Test' and 'Social Interaction Test' will be conducted. A separate group of mice will combine this chemogenetic approach with wireless EEG-transmitters to validate forceps minor inhibition and assess brain activity in relation to social behavior in freely interacting mice.

Results
Behavioral recordings are currently in progress, and data collection is ongoing.

Conclusion
This study aims to provide insights into the causal relationship between forceps minor activity and social behavior. Further interpretations can be drawn upon the completion of data analysis.

8

The Pearls and Perils of 'Friendship as Method' in Psychosis Inquiry

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prof. dr. Richard Bruggeman[1]

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Background
Communications and collaborations with and around people with psychosis in supportive housing contexts entail many difficulties. Our study aim was to gain more insight in important issues regarding these communications and collaborations, starting with people with psychosis themselves. We worked with 'friendship as method' (Tillmann-Healy, 2003), an unknown and unusual approach in psychiatric research.

Objective
We aim to methodologically evaluate: (i) Can 'friendship as method' be practiced with people with psychosis?; and (ii) What are the 'Pearls' and 'Perils' of 'friendship as method'?

Design/methods
From August 2020 up until the summer of 2023, encounter-based fieldwork was conducted in supportive housing contexts. Thirteen people with persistent psychosis were my (Alke) key interlocutors – those I mainly conversed with in the field. Other interlocutors were e.g., 16 relatives, 22 supportive housing workers and 10 FACT workers.

Results
The pearls of 'friendship as method': this research approach was overall appreciated by key interlocutors, firstly because of the opportunity to talk about a variety of (fundamental, existential) topics. Secondly, people appreciated the self-disclosure of the researcher. Thirdly, with some of them I was/am actually 'becoming-friends'. Also care workers recognized that people benefitted from this research. We gained unique, intimate and relational insights in the issues of people with psychosis and those close to them, by affectively participating in meaningful moments of (trying/failing to come to) a shared understanding. The perils of 'friendship as method': the responsibility in befriending people in vulnerable positions, various romantic and sexual advances, the 'opportunity' to have intercourse with some of them, the associated boundary-work, the limits to self-disclosure, getting 'sucked into a delusional system', and my 'inimical friendship' to care workers. We highlight what this method demands of the researcher. And how to set-up a safe space of super/intervision in the research team.

Conclusion
Friendship as method is a promising approach in psychosis inquiry, for we gained rich and multi-layered insights in important communication and collaboration issues. This method is emotionally taxing, and it requires reflexivity and a safe atmosphere in the team. This research approach has important 'humanizing' implications for psychiatric practice.

9

Relation between language impairments and verb and sentence processing: the validation of a new diagnostic tool

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Background
Language processing difficulties vary across word types, with verbs posing challenges, especially in children with language disorders. Existing diagnostic tools for Dutch children lack assessment of verb processing abilities related to syntactic properties, such as argument structure, finiteness, and word order.

Objective
This study aims to validate a novel test battery focusing on verb and sentence processing for children (4-12 years). We assess construct validity, by correlating test scores with age and with already existing standardized tests, and examine reliability and diagnostic accuracy. The focus is on word properties and morphosyntactic processes.

Design/Methods
We recruited 90 typically developing (TD) children and 34 children with Developmental Language Disorder (DLD). Both groups underwent language assessments, including a novel test battery and standardized tests, measuring verb production and comprehension, sentence completion, and comprehension.

Results
Current results from the show performance below matched controls in all language tests, with large effect sizes. The psychometric properties of this test are satisfactory, ranging from acceptable to excellent reliability and good construct validity. Furthermore, children with DLD score significantly lower on low-concrete words compared to high-concrete words and demonstrated more grammatical errors than their typically developing peers.

Conclusion
The novel test battery effectively detects verb and sentence processing difficulties, providing insights into specific challenges for children with DLD. At a group level, the challenges observed among the DLD participants in processing low-concrete words suggest a potential disorder in semantic processing. This tool's ability to identify the specific aspects of verb and sentence processing that are most challenging for children facilitates targeted and personalized speech therapy, thus contributing to future research on linguistic outcomes.

10

Brain activation during positive affective forecasting in patients with recent suicidal attempts

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Background
Hopelessness and negative anticipatory biases towards future outcomes are strongly associated with suicidality. Here we aimed to study whether recent suicidal attempters have difficulties in vividly anticipating positive future events and whether distinct neural mechanisms underlie this.

Methods
Baseline data from the HOPES clinical study were analyzed, including three groups, patients with a recent suicide attempt (SP, N = 23), matched patient controls (PC, N = 22), and non-patient controls (NPC, N = 23). During fMRI scanning, participants performed the affective forecasting task to envision personalized positive and neutral future events. Differences on the vividness of the forecasting were compared across groups by using mixed ANCOVA with age and years of education as covariates. Group difference on brain activation during positive affective forecasting was investigated by using one-way ANOVAs. Associations between brain activation, suicidality, hopelessness, and anxiety were evaluated by using linear regression analyses.

Results
SP and PC showed reduced vividness during affective forecasting compared to NPC. Across all participants, envisioning positive events was associated with increased activation in brain regions encompassing the default mode network and limbic areas, coupled with reduced activation in the dorsal attentional network and premotor cortex relative to imagining neutral events. No group differences were observed in brain activation during positive imagery compared to neutral imagery. Both SP and PC exhibited increased activation in the left dorsolateral prefrontal cortex (DLPFC) during forecasting positive events, and increased activation in the left insula, left middle frontal gyrus, and left DLPFC during forecasting neutral events relative to NPC. Higher levels of hopelessness were associated with higher suicidal ideation, and reduced activation in the orbitofrontal cortex and the frontopolar cortex during positive imagery compared with neutral imagery within SP compared with PC. Additionally, anxiety symptom severity was positively associated with brain activation in the superior medial frontal gyrus within PC, but negatively within SP group. Results were independent of the persistence of psychiatric disorders, severity of depressive symptoms, and the use of medication or psychotherapy.

Conclusion
This study suggested that deficits of forecasting future events may be more related to psychopathology, but not specifically to suicide vulnerability. Feelings of hopelessness and anxiety symptoms may interact with the neural underpinnings of biased affective forecasting, which can lead to suicidal behavior. The psychopathological pathways underlying suicidality require further study.

11

Lexical access in adolescent second language learners: Evidence from behavioral lexical decision and directions for future psychophysiological research

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Background

Language co-activation of two or more languages in multilingual speakers is a widely researched topic. One type of word that has frequently been used to examine cross-linguistic influences on lexical processing is cognates, that is translation equivalents sharing the same/similar form and meaning across languages (e.g., English-German *summer-Sommer*). Cognates are typically processed faster and more accurately by bilinguals than noncognates, that is translation equivalents without such overlap (e.g., English-German *beach-Strand*). This processing advantage of cognate words is considered evidence for co-activation of languages and thus language non-selective access in bilingual language processing.

Objective

Previous research on bilingual language processing has revealed simultaneous coactivation of first (L1) and second (L2) language during bilingual word recognition in adults (Dijkstra et al., 2010) as well as children (Gastmann & Poarch, 2022). However, few studies have investigated cross-language activation in adolescents. To fill this gap, the present study explored L2 word recognition and its potential modulating factors in adolescent second language learners.

Design/methods

Fifty-eight L1 German low-intermediate learners of L2 English (age: M = 13.4, SD = 0.7) performed an English Lexical Decision Task on cognate and noncognate words and completed the Peabody Picture Vocabulary Test (PPVT; Dunn & Dunn, 1997) as a measure of their L2 English proficiency.

Results

Contrary to our predictions, cognate effects could not be replicated in either accuracy or reaction time (RT) data. Post-hoc analyses, however, revealed that cognate processing was modulated by word frequency and learners' L2 proficiency. Linear mixed effects RT analysis revealed a three-way interaction (p = .049) of cognate status, L2 proficiency, and word frequency (SUBTLEX-Lg10; Brysbaert & New, 2009), with less-frequent items inducing a cognate facilitation effect in low(er)-proficient learners. Similarly, generalized linear mixed models on accuracy yielded marginally significant two-way interactions between cognate status and word frequency (p = .076) and between cognate status and L2 proficiency (p = .063), with cognate effects being restricted to lower-proficient learners and less frequent items.

Conclusion

The present study's results expand previous findings of limited cognate facilitation (e.g., Bultena et al., 2014) to a population of younger learners. The poster presentation will highlight directions for future research and will provide a sneak peek at a follow-up pupillometry study.

12

The barriers and facilitators in using Virtual Reality relaxation for burnout and psychiatric patients: a qualitative analysis

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Background Stress is a transdiagnostic factor in the onset and recurrence of psychiatric disorders and burnout. The Virtual Reality (VR) relaxation tool, VRelax, is a promising tool to aid in relaxation in both the general and mental healthcare population. VRelax offers a diverse range of immersive 360-degree audio-visual nature environment videos and images. Users can explore serene mountain landscapes, engage in underwater adventures such as scuba diving with dolphins, and explore different forest environments. Despite existing evidence supporting the effectiveness of VR relaxation in acute stress reduction, the potential to reduce chronic stress, and improve positive and negative affective states, VR relaxation is still not widely adopted in everyday clinical practice. By prioritizing various perspectives, the implementation of a VR tool in clinical practice will be more successful. However, barriers and facilitators to using VRelax from a patient perspective have not been explored.

Objective This study aims to investigate patient-perceived barriers and facilitators to the use of VRelax to optimize the experience.

Design/methods In May and June of 2021, five focus groups were conducted. Participants were recruited via the network of patient representatives, healthcare professionals, and social media. Semi-structured interview guides with open-ended questions were used to investigate the barriers and facilitators. The focus groups were audiotaped, transcribed verbatim, and analysed using ATLAS.ti 23.2.3. Barriers and facilitators were identified using thematic analysis from Clark and Braun (2006).

Results There were 12 patients with burnout or psychiatric disorders in five focus groups. Participants ranged from two to five per group. Thematic analysis identified eight themes: two facilitators (conducive social setting, enhancing autonomy), three barriers (physical discomfort, short-comings (initial) guidance, the transition phase back to reality is missing), and three that are both barrier and facilitator (ease of use, immersive factors, perceived usefulness) in the use of VRelax.

Conclusion The present version of VRelax should be more tailored to align more seamlessly with the individual requirements and needs of patients with burnout and psychiatric disorders. More attention should be given to improving the usability and user-friendliness of VRelax to increase the experience and for the promotion of the facilitating factors, such as the positive influence of social environment and the high autonomy in the use of VRelax.

13

Deciphering the heterogeneity of brain disorders in relation to complex genetics

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Background
From the 20th century, case-control studies stand as the benchmark in brain research, where patient diagnosis, relying on either neuropathology or clinical history, serves as the sole criterion. With such an approach, you sacrifice a significant amount of information because of substantial intragroup differences and heterogeneity.

Objective
In light of these concerns, we suggest adopting a holistic method to thoroughly investigate the data modalities related to neuropathology, genetics, and clinical information and their interconnections to refine our understanding of the etiology of brain disorders.

Methods
This project is going in collaboration with the Netherlands Brain Bank (NBB), which has performed more than 4500 brain autopsies of donors with and without brain disorders. During the first phase of the project, Mekkes et al. 2022 extracted, standardized, and analyzed detailed clinical reports of 3042 NBB donors encompassing 84 neuropsychiatric signs and symptoms identified through Natural Language Processing. The ongoing part of our research is focused on genetics and omics analysis of patients' data along with processing the neuropathology reports. The key idea is to analyze symptom- and neuropathology-specific clusters aiming to find out how the underlying genetics affect disorder manifestation. Integrating omics data of the mental disorders' part of the cohort will allow us to establish associations between observed genetic variations and the dysregulation of specific transcription factors in the psychiatric disorders.

Results
To explore clinical and general pathological information and corresponding ontologies built in our project, visit nnd.app.rug.nl

Conclusion
Extending brain research with the study of genetics, neuropathology, and clinical symptomatology might be a key to unlocking the mysteries of brain disorders heterogeneity. By bridging these dimensions, we can forge a more comprehensive understanding, ultimately paving the way for innovative approaches to diagnosis, treatment, and prevention in the realm of neurodegenerative and psychiatric health.

14

Modifying TDP-43 Toxicity

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Background
Protein toxicity is thought to underlie several, yet incurable, age-related neurodegenerative diseases, including Amyotrophic Lateral Sclerosis (ALS). TDP-43 aggregation is the major pathological hallmark of ALS and present in 97% of all cases, suggesting that TDP-43 contributes to the disease mechanism. How protein toxicity triggers cell-and physical dysfunction and leads to degeneration is still not understood.

Objective
The aim is to to study biological mechanisms that lead to disease-related phenotypes and find modifiers for TDP-43 induced toxicity using a *C.elegans* model.

Design/methods
For this aim, we carried out a whole genome RNA profiling and found that genes involved in calcium ion binding, ion channels, muscle function and post-synaptic reception were upregulated. Then we did a compound screen that targeting different ion channels in *C.elegans.*

Results
Our the whole-genome RNA profiling revealed significant changes in genes related with calcium ion binding, ion channels and post-synaptic reception. Following experiments showed that activation of L-type calcium channels or inhibition of calcium-activated large-conductance BK potassium channels could rescue the movement defects in TDP-43 worms.

Conclusion
In conclusion, our exploration into the mechanisms underlying TDP-43-induced toxicity in a *C. elegans* model has revealed intriguing insights. Our research offers promising avenue for further research into ion channels and their importance in neurodegenerative diseases, particularly ALS.

15

Patterns of emotion recognition in various neurological disorders

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Introduction: Social cognition disorders can develop after brain damage. Impairments in aspects of social cognition, including emotion recognition, are disorder-transcending and can occur in various neurological disorders such as traumatic brain injury (TBI), stroke (including cerebrovascular accident (CVA) and subarachnoid haemorrhage (SAH)). It is, however, not known if and how patients differ with respect to the extent to which overall emotion recognition as well as recognition of the specific subtypes of emotions (anger, disgust, fear, happiness, sadness, surprise) are impaired. The aim of this study, therefore, is to investigate if and how various neurological patient groups diverge in their pattern of emotion recognition.

Methods: In this study, patients who suffered from three types of serious neurological disorders were included. Included were: patients with moderate-severe TBI (N = 118; age M = 37.8, SD = 13.7), CVA patients graded 5 or higher on the National Institutes of Health Stroke Scale (NIHSS) (N = 100, age M = 64.9, SD = 10.6) and patients with aneurysmal SAH (N = 121, age M = 54.2, SD = 10.8). Emotion recognition was measured with the The Facial Expression of Emotion-Stimuli and Test (FEEST) in which patients' ability of recognizing 60 pictures of faces with emotional expressions representing the six basic emotions; (ten of each) was tested. FEEST scores were compared to normative data (median) by means of a One-Sample Wilcoxon Signed Rank Test. Different patient groups were compared on emotion recognition by Independent-Samples Kruskal-Wallis Tests.

Results: Results showed that each patient group scored significantly lower on overall emotion recognition compared to the normative group: all groups ($p < .001$). Moreover, on overall emotion recognition, we found that the TBI group and the CVA group scored significantly lower than the SAH group ($p < .05$) . Furthermore, we found that these neurological disorders significantly differ in recognizing specific emotions. Patients with TBI and patients with CVA scored significantly lower on recognizing sadness than patients with SAH ($p < .05$). Moreover, CVA patients scored significantly lower on recognizing surprise compared to patients with SAH ($p < .05$).

Conclusion: This study shows that impaired emotion recognition is present in various neurological patient groups and is, indeed, disorder-transcending. However, there are differences in severity of impaired emotion recognition between neurological disorders but the pattern between the disorders seems similar. These differences are important to take into account in clinical practice. In this way, patient care and neuropsychological treatments can be more personalized and adapted to patients' impairments and needs, having a positive influence on treatment outcome.

16

Brain-first versus body-first Parkinson's disease - Does asymmetry matter?

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Introduction
Parkinson's disease (PD) is characterized by a progressive lossof dopaminergic neurons in the substantia nigra. Recent literature has proposedtwo subgroups of PD. The "body-first subtype" is associated with a prodromeof isolated REM-sleep Behaviour Disorder (iRBD) and a relatively symmetricbrain degeneration. The "brain-first subtype" is suggested to have a more asym-metric degeneration and a prodromal stage without RBD. While it would be of pathophysiological and clinical interest to use the degree of asymmetry as a marker to identify PD subtypes, conflicting results are to-date available in this regard. This study aims to investigate the proposed difference in symmetry of the degeneration pattern in presumed body and brain-first PD subtypes.

Materials and Methods
We analyzed [123I]-FP-CIT (DAT SPECT) and 18F-FDG PET brain imaging in three groups of patients (iRBD, n = 20, de novo PD with RBD as a prodromal stage, n = 22 and de novo PD without RBD, n = 16) to assess whether the groups differ in terms of dopaminergic or glucose metabolic symmetry. The RBD-status of all patients was confirmed with video-polysomnography.

Results
The PD groups did not differ from each other with regards to relative asymmetry of DAT uptake in the putamen (AIput, $p = 1.0$). The iRBD patients with an abnormal DAT SPECT scan (iRBDpath), PDRBD+, and PDBRD- did not differ from each other considering the absolute difference between left and right putamen DAT binding ratio ($p \geq 0.08$), while the iRBD patients with a normal DAT SPECT scan were more symmetric than PDRBD+ ($p = 0.002$). The patient groups also did not differ from each other with regards to symmetry of expression of the PD-related metabolic pattern (PDRP) in each hemisphere. The PD groups had no difference in symmetry considering mean FDG uptake in left and right regions of interest, and had the same degree of symmetry as controls (apart from two regions for PDRBD+), while the iRBD patients had nine regions with abnormal left-right difference ($p < 0.001$).

Conclusions
Our findings do not - in contrast to the predictions of the model – support the asymmetry aspect of the "body-first" versus "brain-first" hypothesis.

Keywords: PD, iRBD, 18F-FDG PET, [123I]-FP-CIT SPECT, asymmetry

17

Computational Mechanisms and distinct effect of apathy and anhedonia on Effort-Based Decision Making in adolescence with depression

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Background
Apathy is a syndrome of reduced motivation that frequently occurs in neurological and psychiatric diseases, which is highly correlated with anhedonia, while the underlying mechanisms remain to be established.

Objective
This study used computational methods to investigate the distinct effects of apathy and anhedonia on effort-based decision-making in adolescents with depression.

Design/methods
Thirty-nine adolescents with depression and 50 matched healthy controls performed a physical effort-based decision-making task. Participants accepted or rejected to exert different levels of physical effort (small or large number of key presses) to obtain different magnitudes of rewards or avoid loss. Participants' choices and response times were analyzed by means of a discounting model and a drift-diffusion model.

Results
Across participants, higher apathy levels were associated with reduced willingness to exert effort to obtain rewards, slower information accumulation ability, and longer response times. Apathy and anticipatory anhedonia (rather than consummatory anhedonia) negatively predicted participants' acceptance rates. Moreover, anticipatory and consummatory anhedonia showed opposite effects on participants' information accumulation ability.

Conclusion
Our findings indicate a diminished sensitivity to rewards and distinct effects of apathy and anhedonia on effort-based decision-making in adolescents, highlighting motivational deficits as a potential early diagnostic marker for depression in adolescence. Furthermore, the use of computational modeling sheds light on hidden processes, offering valuable insights into the effects of psychiatric conditions on decision-making processes in adolescence.

18

RESTORE: a prospective repeated measures cohort study of the impact of resilience to stress on recovery from depression

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Background
In individuals with depressive disorders, physiological and psychological stress response is altered. Stress response is an indicator of mental health and resilience, making it an important research target. To investigate stress response, the Trier Social Stress Test (TSST) is a standardized laboratory method of exposure to a social stressor. The virtual reality variant (TSST-VR) circumvents challenges faced by the standard TSST to provoke social stress under identical experimental conditions, with minimal personnel.

Objective
The primary aim is to identify whether indices of stress response evoked by the TSST-VR predict depression symptom severity measured by the Inventory of Depressive Symptomatology - Self Report (IDS-SR) in the short and long term, in adults treated for a depressive disorder.

Design/methods
Stress response to the TSST-VR will be assessed at baseline. Backwards multivariable linear regressions will assess the best predictive models for change in depressive symptom severity at 5 time points respectively, with IDS-SR score as the outcome and stress response variables as potential predictors. Covariates include factors that may influence stress response, such as chronicity, childhood maltreatment and comorbid anxiety.

Results
An optimal stress response allows adaptation to the environment and anticipation of future challenges, and a disproportionate stress response in either direction may be maladaptive. Thus, a curvilinear relationship between stress response magnitude and symptom severity at follow-up is expected, such that blunted or exaggerated stress response predict worse treatment outcome. Childhood maltreatment and chronicity may explain a blunted stress response, while comorbid anxiety could explain an exaggerated stress response. A multimodal approach should improve predictive value and aid in the identification of a candidate resilience marker.

Conclusion
The use of VR software to assess resilience in a depressed population will form the basis for identification of a multimodal resilience marker that could predict disease outcome and treatment response. VR tools can unlock access to any environment without leaving the lab or clinic, and offer meaningful advantages over standard assessment tools in terms of reliability, repeatability and ease of use. On the horizon, VR tools could improve methodological rigor in research, and facilitate accurate and individualized diagnostic and prognostic assessment.

19

Language learning to boost episodic memory in older adults with and without suspected cognitive impairment

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Background
Atrophy of brain structures critical for episodic memory function is associated with a higher risk of progression from healthy aging to cognitive impairment and from the latter to Alzheimer's dementia. Crucially, these structures can change in volume and function as a result of behavioral interventions in older adulthood, sometimes leading to behavioral improvements in episodic memory. Language learning has potential to boost episodic memory in older adults with and without suspected cognitive impairment (CI and non-CI), stemming from the involvement of the episodic memory brain structures in this cognitive exercise. However, not much is known about the impact of language learning on episodic memory in older adults.

Objective
This poster will present preliminary results of an intervention study investigating the cognitive effects of language learning in older adults with varying levels of cognitive decline.

Design/methods
Functionally monolingual Dutch older adults with suspected CI (*n* = 13) or non-CI (*n* = 15) completed a three-month online English course consisting of intensive self-study and online bi-weekly group lessons. Participants were classified as having CI when they reported a diagnosis of Mild Cognitive Impairment *or* if they reported subjective cognitive decline and scored below the recommended Montreal Cognitive Assessment cut-off point of 25/26. Episodic memory was assessed at pre-test, post-test, and four-month follow-up using the Visual Association Test-Extended (VAT-E), with associative memory and free recall performance as the main outcome measures.

Results
Our results demonstrated that both groups improved associative memory and free recall performance from pre-test to post-test to a similar extent. Crucially, these improvements were maintained at follow-up, after several months of not engaging with language learning. The CI group performed lower on associative memory than the non-CI group at pre-test, but this difference disappeared at post-test, suggesting that the group with suspected CI approximated normal performance after having participated in the language learning intervention.

Conclusion
A complex activity such as language learning can positively affect episodic memory in older adults who appear to age healthily as well as in people with suspected cognitive impairment. As such, language learning could be a promising healthy cognitive aging tool to boost episodic memory and perhaps prevent or postpone the progression to cognitive impairment or dementia.

20

Telediagnosis of executive functions by new test battery utilizing dual mechanisms of cognitive control

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Background
Executive functions (EF) are higher cognitive functions that enable adapted goal-oriented behaviour, emotional and motivational regulation, and cognitive functioning (Barkley, 2012). Their healthy interplay is fundamental for successful everyday life and autonomy. Deficits in EF are associated with many psychopathological and neurological conditions. New EF assessment methods are urgently required to apply new theoretical frameworks for more precise EF diagnosing and training.

Objective
In our study we aimed to develop novel EF tests in online environment that systematically cover four core components of EF – conflict monitoring, set shifting, inhibition, and working memory updating (Friedman & Miyake, 2017), and that apply theoretical concept called dual mechanisms of cognitive control (Braver, 2012), whose monitoring brings important information that can provide broader insight about one's executive functioning.

Design/methods
OpenSesame software (Mathôt et al., 2012) was used to create our EF test battery in proactive and reactive cognitive control mode modification that is applicable for on-line measurements. Ninety-two healthy, English speaking participants (71 female, 21 male) in the age range 18-60 ($\tilde{x}$ = 36.7) years were measured online. We used the Pearson correlation to compare executive functioning in everyday life reported in BRIEF-A with the performance in the test battery. In each of our 4 tests we measured reaction times and accuracies in both executive conditions, cognitive control mode, and their interactions. We used ANOVA tests to statistically examine differences for each task's performance measures.

Results
In EF condition we found statistically significant difference between reaction times and accuracies in all EF tests. In cognitive control mode we found significant difference mainly in reaction times during conflict monitoring, set shifting and inhibition task. In conditions interaction, we found significant differences only in conflict monitoring and set shifting task. We found no significant correlation in total reaction times and accuracies in EF tests and BRIEF-A global executive composite score.

Conclusion
The EF test battery run in the online environment satisfactorily and made the testing faster and more efficient. The measured effects of EF and cognitive control modes are in expected direction, more consistent and larger effect sizes are observed in the EF dimension. The association between subjective and objective measures proved not to be significant.

21

Mind Your Arteries: Coronary Artery Calcium and Alzheimer's Disease Biomarkers in Cognitively Unimpaired Adults

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Background
Atherosclerosis, the hardening of arterial walls due to gruels or paste resulting in atherosclerotic plaques, is linked to cognitive dysfunction in cognitively unimpaired individuals and an increased risk of dementia and cognitive decline. Findings on the impact of high coronary artery calcium (CAC), a subclinical atherosclerosis biomarker, on cognition remain inconsistent. Additionally, its effect on Alzheimer's Disease biomarkers has not been previously analysed.

Objective
This study explores differences in cognitive measures and Alzheimer's disease biomarkers in cognitively unimpaired adults with low or high subclinical atherosclerosis. The final aim is to identify groups at higher risk of cognitive decline and to validate early markers of cognitive decline.

Design/methods
285 cognitively unimpaired adults over fifty were recruited through the Lifelines database, a population-based cohort study in the Netherlands. Participants underwent cardiac computerised tomography to derive total CAC using the Agatston score. Participants were categorized into low CAC (score 0, n=154) and high CAC (>300, n=131). Subsequently, they underwent a neuropsychological assessment and blood was sampled. Domain scores were created for memory, executive functioning, information processing, manual dexterity, and general cognition. Serum Alzheimer's disease biomarkers (Aβ40, Aβ42, pTau181, NfL, GFAP) were analysed using a single-molecule array assay technology. Group differences between low and high CAC group were analysed using ANCOVA models adjusting for main confounders and correcting for multiple comparisons.

Results
After excluding participants with MMSE < 25, 278 participants (68 ± 9 years, 59% males) remained. The high CAC group, older and with more males, exhibited worse memory ($p < .001$), executive functioning ($p < .001$), information processing ($p = .006$), manual dexterity ($p < .001$), and overall cognition ($p < .001$) compared to the low CAC group. Higher pTau181 levels were observed in the high CAC group ($p = .032$). No differences were found for all other determined Alzheimer's disease biomarkers ($p > .050$).

Conclusion
Our results suggest that subclinical atherosclerosis is associated with a higher risk of cognitive decline, as evidenced by poorer cognitive function and elevated pTau181 levels. Extensive brain MRI data has also been acquired to assess both brain structural and functional characteristics of these groups. Ongoing investigations aim to validate early cognitive decline imaging markers and explore the relationship between cerebrovascular and Alzheimer's disease markers in this population.

22

Iron(ing) out neurodegeneration: targeting ferroptosis pathways to unravel novel research techniques and therapeutic avenues in tau-related parkinsonisms

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Background

Parkinsonism is a spectrum of neurodegenerative disorders, characterised by motor-related deficits, caused by degeneration of dopaminergic neurons in the substantia nigra (SN). Although Parkinson's disease (PD) is the most common type of parkinsonism, definite diagnoses are only possible post-mortem which, due to the clinical similarity of different parkinsonisms, often leads to misdiagnoses. In this project, we focus on Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) parkinsonisms, and their pathological hallmark, tau. Both alpha-synuclein (aS), PD hallmark, and tauopathies have been linked to ferroptosis pathways. Ferroptosis is a non-apoptotic, iron-induced, form of cell death, thought to be linked to age-related neurodegenerative diseases and thus, exploring its underlying mechanisms could further our understanding of PSP/CBD pathophysiology.

Objective(s)

(1) Improve research from a technical point by fine-tuning a new tool, digital spatial profiling (DSP), in post-mortem tissues and, for the first time, explore spatial transcriptomics in dopaminergic neurons with *and* without pathological inclusions.
(2) DSP will consequently deepen our understanding of ferroptosis-related pathways at a molecular level.
(3) Study ferroptosis-related markers in relevant cell lines with a novel tau-protofibril model and (3) intervene via pharmacological manipulation of ferroptosis.

Design/methods

The ferroptosis pathway will be quantitatively evaluated in human post-mortem SN surviving neurons with *and* without tau, using DSP. The relationship between tau and ferroptosis will also be tested in primary neurons and differentiated dopaminergic neurons with tau-protofibrils, using pharmacological ferroptosis inhibitors/stimulants, to evaluate viability and tau accumulation.

Preliminary results and impact

In support of the DSP novel approach, preliminary data using pixel density scoring indicated differential expression of ferroptosis-related markers in tau-labelled neurons within the SN of post-mortem PSP/CBD brains, compared to age-matched controls and PD patients. However, it is still unclear if pathology is a *cause* or a *consequence* of ferroptosis in the progression of parkinsonism. Analysis of the ferroptosis pathway *in vitro/vivo* will help understand the relationship between ferroptosis and tau in PSP/CBD progression. Furthermore, comparing the output of tau with existing aS data will help elucidate differences (and commonalities) between parkinsonisms at a molecular level.

Conclusion

Ferroptosis seems to be a key component of parkinsonism progression and a possible target for novel therapeutic avenues. Hence why we study ferroptosis in surviving/live neurons which will offer insight into which components could confer this cell death resilience, despite ferroptosis machinery being seemingly active. As previously mentioned, tau-related parkinsonisms are often overlooked due to their clinical similarity to PD, consequently leading to misdiagnoses and the regression in funding/research of PSP/CBD, ultimately leaving patients without adequate care. Thus, with our state-of-the-art approach, it is our hope that the findings of this project will reveal new research methods to study neurodegeneration and ferroptosis, as well as unravel novel aspects of parkinsonism pathophysiology.

23

Cellular heterogeneity in the development and progression of MS brain lesions

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Background
Multiple sclerosis (MS) is an inflammatory neurodegenerative disease of the central nervous system (CNS) that affects over 2 million people worldwide. In MS, the myelin that ensheaths axons is targeted for degradation, which leads to neurodegeneration. The affected areas in the brain – lesions – are classified in various types (pre-active, active, mixed, inactive, remyelinated) that are thought to share a temporal component and progress over time. The pathophysiology of MS is highly heterogeneous with regard to lesion localization, progression, and involved cell types. Both CNS-resident cells and infiltrating immune cells play important roles in lesion initiation and evolution. What factors trigger the development of these lesions and their progression is not yet known.

Objective
In this study, we address the heterogeneity of all cell types and their (altered) interactions in the different MS lesion types to better understand lesion progression.

Design/methods
We identified altered gene expression patterns of cellular subsets in different MS lesions using single-nucleus RNA-sequencing (snRNA-seq) on human post-mortem white and grey matter tissue.

Results
Preliminary results indicate a changed cellular heterogeneity between MS and control CNS tissue, and between the different MS lesion types. Gene expression patterns of the major glial cell types – microglia, astrocytes, and oligodendrocytes – were altered in MS. Moreover, vasculature cells and immune cells were enriched in specific white matter lesion types and had altered interaction patterns.

Conclusion
Thus, cellular heterogeneity and gene activity are contingent on lesion progression, or vice versa. Further in-depth analysis of lesion-type enriched cellular subsets, the involved genes, perturbed interactions and pathways will be presented. Together, these factors could aid in delineating the processes that drive MS lesion evolution, and might offer novel targets to modulate disease progression or promote remyelination.

24

iPSC differentiation to microglia and dopaminergic neurons to study brain intercellular interactions in Parkinson's Disease

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Background
Parkinson's Disease (PD) is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons in the substantia nigra, leading to motor impairments. Recent research has highlighted the crucial role of microglia, the resident immune cells of the central nervous system, as microglia-mediated inflammation and dysfunction could be implicated in the degeneration of dopaminergic neurons in PD. The Leucine-Rich Repeat Kinase 2 (LRRK2) G2019S mutation is the most common genetic risk factor for PD and is associated with neuro-inflammatory processes.

Objective
We aim to study the role of LRRK2 in the function and communication between dopaminergic neurons and microglia and how this can contribute to the neurodegeneration found in PD.

Design/methods
Research on brain cells can have its limitations as human samples can only be obtained post-mortem and murine models don't fully recapitulate the human pathology. Patient-derived induced pluripotent stem cells (iPSCs) provide a valuable model to obtain human brain cells.
Our approach involves differentiating patient-derived iPSCs carrying the LRRK2 G2019S mutation into microglia and dopaminergic neurons to elucidate the interaction and communication between the two cell types in the context of PD.

Results
We successfully differentiated iPSCs from 3 different cell lines - Gibco (healthy control), LRRK2 G2019S mutated and LRRK2 isogenic control – into mature microglia (IBA1+ and TMEM119+) and dopaminergic neurons (TH+). The LRRK2 G2019S mutation led to altered expression of TH+ and interestingly also VDAC+ suggesting the involvement of mitochondria. The metabolic activity of the microglia carrying G2019S mutation was also changed compared to isogenic cells.

Conclusion
The generated iPSC-derived microglia and dopaminergic neurons can be used to study cell-cell interactions and communication and the involvement of LRRK2 in the context of PD.

25

"Why were you speeding?": A Self-Confrontation Study on Awareness and Reasons for Speeding Behaviour

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Background
Despite extensive speeding prevention efforts, including legislative enforcement, road design adaptations, and technologies like adaptive cruise control, speeding remains a large contributor to traffic casualties (Breen et al., 2020). While speeding has been associated with demographic specificities (e.g., being male and young, Høye, 2020) or specific motivations (driving for fun, Ahie et al., 2015), understanding drivers' awareness and subjective reasons for speeding could enhance intervention strategies.

Objective
This study aims to develop more nuanced intervention strategies by focusing on two key aspects: (1) drivers' self-awareness regarding their speeding behaviour and (2) the subjective reasons they provide when reflecting on this behaviour. Awareness is crucial for identifying the need for educational support to improve self-assessment among drivers. Similarly, understanding the reasons drivers articulate for their speeding behaviour can serve as potential focal points for tailored risk-reduction initiatives.

Design/methods
To investigate these two topics, a self-confrontation study (see Mollo & Falzon, 2004) was conducted: 25 participants recorded one of their usual drives, using GoPro cameras, capturing both the road view and their speed. Selected video segments were later reviewed with participants, focusing on their awareness of speed behaviour, either within the limits or above, and the underlying reasons for their speed choice. The study also explored general attitudes towards speeding, perceptions of its problematic nature, the acceptability of exceeding speed limits, and decision-making in speed choice.

Results
The study revealed that most drivers who exceed speed limits are aware of their behaviour, often attributing it to habitual driving patterns, perceived safety, or the need to match the flow of traffic. The majority of observed speeding instances were less than 10% above the limit, often rationalized by drivers as 'normal' in comparison to the behaviour of other road users. Conversely, drivers who adhered to speed limits typically cited a straightforward preference for rule-following, without feeling the need for further justification.

Conclusion
The study observed a spectrum of behaviours, from dangerous excessive speeding to strict adherence to speed limits. However, the most prevalent pattern was 'normal' speeding, defined as exceeding the limit by a few kilometres per hour. This behaviour suggests the existence of a 'normal illegal' zone (Amalberti et al., 2006) in driver perceptions of speeding, which is crucial for understanding and improving the effectiveness of road safety interventions.

26

‘No Guts, No Glory’: The efficacy of an anti-inflammatory diet on improving global functioning, gut (health), and microbiome of people with a brain disorder – study design

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Background
People with bipolar disorder (BD), schizophrenia spectrum disorders (SSD), and Parkinson’s disease (PD) are suffering from severe symptoms affecting their functioning and quality of life. Elevated systemic inflammation, stemming from increased intestinal permeability, significantly affects brain functioning through the gut-brain axis. Gut health offers a promising window of opportunity for therapeutic intervention, with an anti-inflammatory dietary pattern slowing deterioration of these brain disorders.

Objective
Investigating the efficacy of an anti-inflammatory diet on improving global functioning, (gut)health, and microbiome of patients with BD, SSD, and PD.

Design/methods
Randomized controlled open-label trial with a cross-over diet intervention lasting 12 weeks and a 24-week wash-out period. The study population consists of patients with SSD (n=25), BD (n=25), and PD (n=49). Patients are either randomized to group 1, starting with the Brain Anti-Inflammatory Nutrition (BrAIN) diet after baseline period 1 (week 1) or group 2, starting with the BrAIN-diet after baseline period 2 (week 36), 1:3 respectively. During the 12-week intervention patients receive free food boxes for a complete dietary pattern, weekly. Moreover, recipes, cooking videos, and weekly dietary consults are provided. Outcome measurements are assessed once every three months, for a total of 6 visits (V1-V6). Primary outcome is global functioning assessed with Outcome Questionnaire 45 (OQ-45). All visits occurred at the patient's home or at UMC Groningen.

Results
Recently, the last participant was included. Therefore, preliminary results of the intervention were yet not available during abstract submission. The study population includes 57 male and 42 female participants. Already 35 patients finished the study, and almost 60 patients completed the BrAIN-diet intervention. Baseline results are expected this spring.

Conclusion
Based on interviews, most patients reported improvement in well-being and (physical) health after finishing the BrAIN-diet intervention. However, since the study is still ongoing, we cannot draw firm conclusions yet.

27

Verb processing and verb learning in children with posterior fossa tumors

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Background

Intracranial tumors are the most frequent pediatric solid neoplasms (Dörner et al., 2007), and posterior fossa tumors (PPFTs) account for 60% of the cases (Pollack et al., 1995). Survival rates have increased over the past decades, however, survivors of PPFTs have reduced rates of academic outcome and employment (Lassaletta et al., 2015). They also have impairments in several language domains (Huber et al., 2007; Lewis & Murdoch, 2011; Riva & Giorgi, 2000), including verbal learning (Kingma et al., 2022). To date, the word learning abilities, and more specifically, verb learning abilities of these children have not been examined. However, vocabulary knowledge is a strong predictor of cognitive and language abilities (Marchman & Fernald, 2008), so more research should be done on the potential difficulties survivors of PPFTs experience in this domain.

Objective

The aim of this study is to explore the verb learning abilities of survivors of PPFTs. By comparing the performance of typically developing children and childhood survivors of PPFTs in learning verbs with a varying degree of semantic and syntactic complexity, we hope to gain insight into the difficulties that survivors of PPFTs experience in development. This will help developing targeted interventions to improve language outcomes and academic and professional potential later in life.

Design/methods

The verb learning abilities of 42 childhood survivors of PPFTs and an equal number of typically developing siblings will be assessed through a novel verb learning task, in addition to background assessments of their verb and sentence production and comprehension abilities. The verb learning task contains items with a varying degree of syntactic complexity using transitive, unergative and unaccusative verbs, of semantic complexity using verbs with a higher or lower degree of concreteness, and of phonological complexity using non-word with a varying number of syllables. After practicing the items in several practice rounds, verbal learning will be assessed through a recognition and a production post-test.

(Predicted) results

Results from the clinical population have not been obtained yet. However, we expect that childhood survivors of PPFTs may perform below typically developing children, with high inter-individual variability in what aspects of verb learning are more impaired. At the poster session, preliminary results for a pilot administration of the novel verb learning task will be presented from the group of typically developing children. These results reveal that the production post-test is sensitive enough to detect individual differences. In recognition post-test a ceiling effect was found in older children.

Conclusion

Based on the preliminary results from the group of typically developing children, some adaptations need to be made to the task. This entails among other things adding more distractors to the recognition task to render it more sensitive to individual differences.

28

Pilot study - sports intervention to promote social participation in early psychosis

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Background
Individuals in an early phase of psychotic disorder face significant challenges in societal participation. There is a high likelihood that they discontinue work or studies, participate less in social activities, and have reduced contact with peers. (Self)stigma, social exclusion, and physical health problems contribute to these difficulties.

Objective The pilot tested an intervention with the aim of promoting the societal participation of this group through sports and assessing the correctness of the developed research design.

Method The intervention consists of 20 weekly sessions and is personalized and phased: Phase 1 - individual psychomotor therapy (PMT); Phase 2 - group intervention combining PMT and sports; Phase 3 - engaging in sports in the community under the guidance of a community sportscoach. The pilot study comprised three single-case studies with a multiple baseline single-case design, incorporating methods such as the experience sample/diary method (ESM).

Results
In qualitative interviews, all participants expressed positive appreciation for the program. It was crucial that they could work towards personal goals and receive tailored support. Initially, all three participants engaged in sports, but not always in an organized context. Furthermore, the measurements, particularly the high-frequency ESM, proved to be too stressful for one participant, leading to premature cessation. It was also evident that certain topics, such as stigma, could be more thoroughly addressed, and adjustments were made to the quantity of quantitative questionnaires. The overall duration of the intervention was extended to enhance flexibility for the participants.

Conclusion
The intervention, aiming to bridge the gap between sports activities within mental health care and those outside, involving collaboration between psychomotor therapists and neighborhood sports coaches, is well-received by the target group. However, regarding societal participation and social (re)integration, the outcomes vary significantly among participants, making it premature to draw conclusive statements at this point. Both the intervention and research design have been adjusted based on this feedback to facilitate the setup of a new, larger study.

29

Reproducibility of standardized tests for gait, strength and psychomotor speed in persons with Multiple Sclerosis

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Background
The 6-Minute Walk Test (6-MWT), 30 Second Chair Stand Test (30CST), Jamar hand-held dynamometer and Symbol Digit Modalities Test (SDMT) are widely used standardized instruments to assess walking performance, functional lower extremity strength, handgrip strength and psychomotor speed. These instruments have a high test-retest reliability and intra-class correlation (ICC). However, the practice effects are not extensively investigated, while they are crucial when comparing scores at different timepoints in an intervention study testing the effectiveness of a treatment.

Objective
Therefore, the objective of this study was to assess the practice effects in the scores of the 6-MWT, Jamar dynamometer and SDMT in a group of persons with Multiple Sclerosis.

Design/methods
74 persons with MS (aged 27 to 72, *M* = 55.5 years, 19 males) and an EDSS score < 7.0 completed the 6-MWT, 30CST, SDMT and maximum handgrip strength test with the Jamar dynamometer. All tests were repeated with a 1-week interval. We investigated the practice effects using mixed effects models, where subjects were treated as a random factor. Pearson correlations were used to asses test-retest reliability and a one-way model was used to calculate the ICC.

Results
The scores of the 6-MWT, 30CST and the SDMT were higher during the second visit than during the first visit (6-MWT: 348.9.2±3.5 vs 334.2±15.4 meters and 30CST: 8.4±0.2 vs 7.8±0.6 meters and SDMT: 45.5±0.5 vs 42.1±1.4, $p < 0.001$). Furthermore, the handgrip strength of the left hand, measured with the Jamar hand-held dynamometer, was higher during the second visit than during the first visit (34.7±0.4 vs 33.6±1.4, $p < 0.05$). No differences were observed between visits for the handgrip strength of the right hand (35.3±0.4 vs 34.8±1.3, $p = 0.08$). Test-retest reliability was high for all the instruments ($r > 0.90$). ICC was good for the SDMT (0.89) and excellent for the 6-MWT, 30CST and handgrip (> 0.90).

Conclusion
The results show that there is a practice effect for the 6-MWT (clinically meaningful), 30CST, left handgrip strength and SDMT when persons with MS perform these tests with a short (1-week) interval. To minimize the practice effects for these tests, a familiarization session is recommended. For the SDMT, using alternate forms might be beneficial. Furthermore, these findings stress the importance of an appropriate control group, since it is not known after how many repetitions the practice effect will reach a plateau.

30

Effects of early-life stress on social functioning in depression: A systematic review and meta-analysis of rodent studies

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Background
Unfortunately, social difficulties such as dysfunctional social networks, reduced cooperation and empathy, or social anhedonia are common in depressed individuals [1-2]. Preclinical rodent models using early-life stress (ELS) exposure are highly valuable to study the extent to which the trajectory of social functioning deviates in ELS-induced depression-like animal models [3-6]. Yet, a systematic analysis that determines the role of ELS timing (ie., pregestational, prenatal, or postnatal exposure) in the onset of social dysfunction in depression and how early in development the social functioning deviates is missing.

Objective
To systematically analyze the effects of pregestational, prenatal and postnatal ELS exposure on depression-related social behaviors in preclinical mouse/rat models.

Design/methods
We performed a comprehensive literature search in Pubmed and Embase from the first record registered until December 20th, 2023. The search consisted of 3 components: mouse/rat models; pregestational, prenatal and/or postnatal ELS exposure; depression/social behavior. Inclusion criteria in the title/abstract (tiab) screening phase are: 1) original research; 2) mouse/rat model as research subject; 3) the use of pregestational/prenatal ELS exposure that involves maternal stress or postnatal ELS exposure that involves psychosocial stress to the offspring. Inclusion criteria in the full-text screening phase include: 1) no other kind of interventions combined with ELS; 2) research of ELS effects on social behavior of the offspring; 3) inclusion of an untreated control group. After full-text screening phase, extraction of characteristics, extraction of outcome data and categorization of behavioral tests/measures, risk of bias assessment, publication bias assessment, and meta-analyses (if apply) will be conducted.

Preliminary Results
Papers identified through database searching were 5763. After removing duplicates, 4264 papers were included for the tiab screening phase which is currently ongoing. Up to date, 235 papers are included, 213 are excluded, and 52 are pending to discuss with a second reviewer because of different opinions about decision for inclusion.

Conclusion
It is recommended to include papers in the tiab phase based on the criteria of model and the intervention used but not in the outcomes, since behavioral measurements are not always reported in abstracts. We estimate to have a high rate of papers included in the tiab phase, but also have a high rate of papers excluded in the full-text phase as it is likely studies report ELS effects on rodents' behavior but not necessarily in the social domain. Potential meta-analysis may help to elucidate the extent to which the timing of ELS exposure contributes to social impairments in depression and how early the social deviations appear.

31

Unraveling the signaling mechanism behind Plasticity Related Gene-mediated protrusion formation

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Background
The family of Plasticity Related Genes is a group of transmembrane proteins that are part of the Lipid Phosphate Phosphatase superfamily. PRGs are involved in multiple processes in neuronal development. Knockout or downregulation of several PRGs led to an increased sensitivity to seizures and epilepsy (Trimbuch et., al. 2009, Wang et., al. 2021). On the other hand, overexpression of PRG2 (Brosig et., al. 2019), PRG3 (Velmans et., al. 2013, Yu et., al 2015, Broggini et., al 2016) and PRG5 (Broggini et., al 2010, Coiro et., al 2014, Yu et., al 2015) promotes the formation of protrusions at the membranes of both non-neuronal and neuronal cells. These results suggest a role for the PRGs in regulating proper neuronal development and suggest a role in diseases where neuronal development, specifically neurodifferentiation of the dendritic tree, is impaired. However, it is not yet clear how PRGs are regulating these processes and which signaling pathways are involved. Common regulators of morphological changes include components involved in the mTOR pathway such as PI3K/APPL1/Akt (Kumar et., al 2005, Majumdar et., al 2011) Therefore, the mTOR pathway is a good candidate to investigate for involvement in PRG signaling inducing morphological changes.

Objective
The aim of this study is to unravel the signaling mechanisms behind PRG-mediated protrusion formation by focusing on PRG5.

Design/methods
Levels of components of the mTOR pathway were determined using Western Blotting analysis and immunofluorescence after PRG5 overexpressing. To determine the dependence on mTOR for the development of the protrusion phenotype, mTORC1 was inhibited and the amount of protrusions determined in primary hippocampal neurons overexpressing PRG5. Furthermore, we investigated whether neuronal activity is required for the formation of protrusions driven by PRG5.

Results
Overexpression of PRG5 leads to an activation of mTORC1, however, blocking the activity of mTORC1 with rapamycin did not change the amount of protrusions formed after overexpression of PRG5. Formation of protrusions happened independently of neuronal activity.

Conclusion
Although mTORC1 activation is observed after overexpression of PRG5, it is not required for driving the formation of plasma membrane protrusions. Additionally, protrusion formation is independent from neuronal activity.

32

Helicobacter pylori-derived outer membrane vesicles induce astrocyte reactivity and demyelination in organotypic cerebellar slice cultures

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Background
Helicobacter pylori (*Hp*) is a Gram-negative bacterium that colonizes the gastric epithelium of half the world population. In addition to developing gastric diseases, chronic *Hp* infection is a risk factor for extra-gastric pathologies, including neurodegenerative diseases. We previously showed that outer membrane vesicles (OMVs) released by *H*p travel systemically to the brain in a murine *in vivo* model, inducing astrocyte reactivity and neuronal damage *in vitro* and *in vivo*.

Objective
In this study, we evaluated the effect of *Hp* OMVs on axon-myelinating oligodendrocytes in a multicellular environment using *ex vivo* organotypic cerebellar slice cultures (OCSCs, rat) and on myelin membrane forming mature oligodendrocytes in primary oligodendrocyte monocultures (rat).

Design/methods/Results
Following exposure to *Hp* OMVs on OCSCs, astrocytes altered their morphology and increased the expression of astrocyte reactivity marker GFAP. A decrease in the percentage of myelinated axons and the number of Olig2-positive oligodendrocyte lineage cells accompanied this. The latter was attributed to a reduced number of mature CC1-positive oligodendrocytes, while PDGFRα-positive oligodendrocyte progenitor cells remained present, indicating remyelination potential. Unlike lysolecithin-induced demyelination, *Hp* OMVs induced iNOS expression and did not increase the expression of the microglia marker Iba1.
Furthermore, after being exposed to *Hp* OMVs on primary oligodendrocytes, these glial cells decrease the number of the myelin basic protein (MBP) positive cells.

Conclusion
Hence, our findings indicate *that Hp* OMVs induce astrocyte reactivity and demyelination in *ex vivo* OCSCs and *Hp* OMVs directly impact mature myelinating oligodendrocytes *in vitro*. These findings suggest that *Hp* OMVs may contribute to the pathogenesis of demyelinating diseases, such as multiple sclerosis.

33

Peripheral Crowding Magnitude is Similar Under Photopic and Scotopic Luminance Conditions

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Background
Visual crowding is the inability to distinguish a stimulus (target) in the presence of surrounding objects (flankers) and impacts various visual functions. Some of these functions are influenced by the luminance level of the environment, such as visual acuity, and contrast sensitivity. However, the potential interactions between crowding and luminance remain unclear.

Objective
In this study, we explored the magnitude of crowding under five different luminance conditions, ranging from photopic to scotopic levels.

Design/methods
Eight participants were asked to report the orientation of the gap in a white Landolt-C (2°diameter) on a gray background positioned at 10° eccentricity. The target Landolt-C was either presented alone or flanked by four Landolt-C's (2°diameter) placed at one of five center-to-center distances (2°,2.52°,3.22°,4.18°,5.5°). Participants responded by adjusting the orientation of a reference Landolt-C gap (5°diameter) placed at 0° eccentricity. Goggles with neutral density filters were used to manipulate stimulus luminance (0.02 to 200 cd/m²). Landolt-C gap sizes were individually adjusted to equalize acuity performance at isolated levels across luminance conditions. Participants' perceptual error (PE) was calculated based on the difference between their response and the actual orientation of the target gap. Crowding magnitude was defined as $PE_{flanked}$ / $PE_{isolated}$ for each luminance and distance conditions.

Results
Results showed that crowding magnitude was similar under all luminance conditions (BF_{10}=0.23), while a monotonous decrease in crowding magnitude was revealed as the target-flanker distance increased in all luminance conditions. Moreover, participants' PEs were similar in all isolated conditions, confirming similar acuity performances (BF_{10}=0.18).

Conclusion
Our results support the idea that the same neural mechanisms operate under scotopic and photopic conditions for peripheral crowding. Additionally, our results align with prior research on contour interaction in scotopic conditions, suggesting a shared underlying process between contour interaction and crowding.

34

Deciphering the cellular heterogeneity of Frontotemporal Dementia

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Background
Frontaltemporal dementia (FTD) refers to a spectrum of disorders which present as progressive deficits in behavior executive control, motor system or language. It is the second most common neurodegenerative disorder that particularly affects individuals younger than 65 years. 30% of FTD cases is accounted for by autosomal dominant mutation in three genes: progranulin (GRN), microtubule-associated protein tau (MAPT), and chromosome 9 open reading frame 72 (C9orf72). Each genetic group causes between 5-10% of all FTD cases.

Objective
The main aim of current research is to determine the mechanisms that underlie the phenotypic differences, clinical presentation and disease progression of different autosomal dominant mutations that cause FTD (C9orf72 and GRN).

Design/methods
The rare and unique collection of fresh-frozen brain samples in Netherlands Brain Bank enables single nucleus RNA sequencing of FTD brain samples with different mutation. Affected (frontal and temporal) and seemingly unaffected (occipital) regions from FTD brain donors and of age- sex- matched controls will be collected for study. We conducted single-nucleus RNA sequencing (snRNAseq) following 10X protocol.

Results
In total, we had 116 tissue samples from frontal, temporal, occipital, and thalamus with both cortical grey matter and white matter. With FANS sorting, we isolated over 1 million $NEUN^{neg}OLIG2^{neg}$ nuclei, resulting in relatively high numbers of nuclei from low-abundant brain cell types. Unsupervised clustering of the snRNAseq dataset resulted into 13 clusters. Low correlation between cluster gene expression profiles indicated that nearly all clusters represented distinct cell types.

Conclusion
We investigated transcriptomic changes in FTD-GRN and FTD-C9orf72 human brain at the single cell level. Our data indicate that in FTD-GRN, neurovascular unit consists of astrocytes, endothelial cells and pericytes seems to be severely affected. In FTD-c9orf72, different regions showed selectively affected pathology.

35

Do PKU mice possess different social behaviour and circadian phenotypes?

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Background
Phenylketonuria (PKU) is a prevalent amino acid metabolism disease caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH). This deficiency leads to elevated levels of phenylalanine (Phe) in the blood and brain, which can be toxic. This elevated Phe concentration also obstructs the entry of crucial amino acids serving as neurotransmitter precursors into the brain, affecting proper brain function. Although cognitive dysfunction is observed in PKU patients and mouse models, some studies also report that both social-cognitive and sleep functions are affected in these patients. However, there is a limited amount of research conducted on PKU mouse models to understand these aspects more precisely.

Objective
In the present study, we first investigate whether PKU mice show altered social behaviour in the social recognition memory (SRM) test. We then explored the sleep patterns of PKU mice, documenting their wakefulness and sleep cycles, along with their status following sleep deprivation (SD).

Design/methods
Pah^{enu2} mice are chemically induced mutant model which has high Phe levels, similar to an untreated PKU patient. In this study, we used the SRM task to explore the social behaviour in both adult untreated PKU mice and Wild-Type (WT) mice in the C57Bl/6J background. To assess the sleep pattern, passive infrared recording (PIR) and electroencephalogram (EEG) were used to examine the rest-activity patterns in PKU and WT mice. We also attempt to see whether PKU mice display different sleep recovery EEG signals after SD.

Results
Firstly, we found that the untreated PKU mice showed difficulty in social recognition in the SRM test. On rest-awake pattern, PIR data suggests that the PKU mice show different activity patterns during the active phase, abnormal diurnality, and fragmentation. EEG signals indicate that PKU mice demonstrate higher absolute power compared to WT mice in REM, NREM and wakefulness. Strikingly, PKU mice also exhibit previously undetected 'spindle like' signals in all stages of EEG. Currently, we are studying the sleep recovery patterns in the PKU mice.

Conclusion
Our results are the first time to show that PKU mice fail in social recognition in the SRM test. Additionally, our findings also reveal that PKU mice exhibit abnormal sleep-wake patterns, which are currently being further explored through EEG studies.

A1

Studying the link between alpha-synuclein aggregation and ferroptosis in Parkinson's disease as a new therapeutic target

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Background Ferroptosis is a form of non-apoptotic cell death induced by the accumulation of iron-triggered lipid peroxidation. While our cells have inherent mechanisms to maintain homeostasis and counteract ferroptosis, these processes become dysfunctional with age and in age-related conditions such as Parkinson's disease (PD). Other mechanisms, such as protein quality control, also deteriorate as people age, making them more vulnerable to the buildup of pathological protein inclusions like alpha-synuclein, which is a hallmark of sporadic PD. Notably, several markers involved in the ferroptotic pathway have been linked to PD pathology. Additionally, iron buildup in the Substantia Nigra (SN) is correlated with PD development. Free intracellular iron and alpha-synuclein oligomerisation and accumulation seem to influence one another. This mutual interaction may set off a vicious cycle that leads to neurodegeneration. Neuronal cell cultures exposed to soluble alpha-synuclein oligomers produced significantly more ROS. The fact that ion chelators could reduce ROS development in the presence of alpha-synuclein oligomers, but other inhibitors of ROS production could not, suggests that ROS production by alpha-synuclein oligomers is dependent on iron availability. However, the exact relationship between alpha-synuclein aggregation and ferroptosis and how alpha-synuclein aggregation is related to other parts of the ferroptotic pathway is not known yet.

Objective The main aims of the study are (1) to study the interaction between stages of alpha-synuclein aggregation and ferroptosis and to intervene in this process by knock-down of ferroptosis-related markers or by pharmacological inhibition and stimulation of ferroptosis and (2) to evaluate the expression patterns of several ferroptosis-related markers in the SN in different age groups.

Design/methods NanoString GeoMX Digital Spatial Profiling (DSP) will be used to evaluate the ferroptotic pathway transcriptome of dopaminergic neurons in PD patients. The same technique will be used to compare neurons without any alpha-synuclein, neurons with relatively small granular alpha-synuclein inclusion patterns and neurons with large Lewy-body type inclusions. The quantitative assessment will be performed on post-mortem Substantia Nigra (SN) neurons. The findings of this experiment will lead to new hypotheses that will be evaluated both *in vitro* in cell cultures and a C. elegans alpha-synuclein overexpression model.
In vitro experiments will be conducted using dopaminergic LUHMES cells. These cells will be exposed to various forms of alpha-synuclein aggregates, including monomers, oligomers, and protofibrils. The activation of specific components within the ferroptotic pathway will be evaluated. Expression patterns and cell morphology/neurotic network will be compared to LUHMES cells treated with several ferroptosis activators, including Erastin or Sorafinib, RLS3, and Loperamide. In addition, ferroptosis inhibitors such as ferrostatin, Deferoxamine, and ALOX inhibitors will be examined. The findings will help to determine the most effective therapy to treat alpha-synuclein-induced ferroptosis.

Conclusion This study would allow for a better understanding of the link between alpha-synuclein aggregation and ferroptosis. This could lead to novel therapeutic approaches for the development of drugs that interfere in this process, thereby slowing down or ideally stopping disease progression of Parkinson's disease.

A2

Unravelling the interplay between social interaction and sleep in Drosophila melanogaster

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Background Social interactions can greatly influence sleep. For instance, in humans, correlational studies suggest that individuals who engage more in social interactions experience an increased need for sleep. Conversely, inadequate social interactions were associated with decreased sleep quality. However, these studies remain merely correlational and the functional/mechanistic reason for this is still unclear. The effect of social interactions on sleep can be studied using model organisms such as the fruit fly, *Drosophila melanogaster*. Despite being phylogenetically distant from humans, fruit flies, a well-established genetic model, offer a unique lens into the genetic basis of sociality. Moreover, recent evidence has provided substantial proof that flies exhibit a state that resembles sleep at the behavioural and molecular level. Like sleep in mammals, sustained periods of quiescence in *Drosophila* are characterized by increased arousal threshold. Previous research showed that when flies are exposed to increasingly complex social environments for several days, they exhibit progressively higher sleep needs post-social grouping. Additionally, fruit flies exhibit enhanced social interactions during the night when they usually are sleeping.

Objective This project aims to investigate how fruit flies socially interact with each other and how these interactions influence sleep patterns across different group sizes. Therefore, we will quantify and categorise the interactions between fruit flies in a group. Additionally, we will analyse the sleep-wake cycles of fruit flies (Experiment 1). Next, we will vary the group sizes and test how these variations influence sleep-wake cycles (Experiment 2), in contrast to being isolated. Finally, using mutants for the *period* and *clock* genes, we aim to unravel the genes influencing the relationship between social interactions and sleep (Experiment 3). The clock genes and their proteins regulate the sleep-wake cycle by influencing the production and release of various hormones and neurotransmitters. Previous evidence showed that when wildtype individuals are housed with arrhythmic mutants, they showed less synchronous behavioural activity than wildtype individuals. Based on this, the objective is to observe if there is an adaptation of the mutant individuals to the wildtype rhythms or vice versa.

Design/methods The setup will comprise a Raspberry Pi computer with 20 Raspberry Pi cameras recording the flies which will be hosted in bowl-shaped arenas to ensure that flies always present their top side to the camera. The individual flies will be tracked using Trex, an open-source machine learning-based tool. The output will be processed with an in-house python script to quantify social interactions and sleep over time. Social interactions will be quantified based on the criteria defined by Schneider et al. For sleep quantification, we will employ an algorithm that combines the standard criteria for behavioural sleep in flies with specific postures indicative of sleep and rest. Traditionally, a fly is inferred to be asleep when it is inactive for at least 5 minutes, as this time frame of quiescence is associated with an increase in arousal thresholds. The preferred position is described as slightly prone, with the body close to the ground. Sleep is quantified at 30-minute intervals using combined outputs from TreX and the in house python script that uses criteria mentioned above. Mutants for the *period* and *clock* genes will be used.
Personally, I will perform the behavioural experiments and analyze the data using Trex and the in-house python script to quantify social interactions and sleep in wildtype and mutant flies.

Conclusion Exploring communal sleep in Drosophila melanogaster offers a unique opportunity to understand the benefit of group living observed in most species. The genetic tractability and well-characterised neural circuits of Drosophila will illuminate the evolutionary advantages and mechanisms of communal sleep, potentially informing our understanding of this process in other species. Using mutants for specific circadian genes will allow a deeper understanding of how differences in circadian rhythms may exert an influence on the interactions between individuals. Ultimately, this research seeks to elucidate the adaptive significance and mechanisms of communal sleep behaviours, emphasising the interplay between sleep and social dynamics.

B1

Long Term Consolidation: Can We Find Memory Markers in the EEG Signal?

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Background: Long-term memory (LTM) is crucial for retaining and retrieving knowledge and experiences, influencing learning, decision-making, and identity. Memory encoding and retrieval are well-studied. However, the intermediate phase that involves consolidation is less understood.

Electrophysiological markers, suggest a link between specific EEG patterns and memory consolidation. For example, sleep spindles and EEG oscillations have been identified as markers for the consolidation process (Petzka et al., 2021; Creery et al., 2022). Therefore, highlighting the importance of EEG markers in understanding memory retention and forgetting mechanisms. These slow oscillatory EEG rhythms also play a key role in memory consolidation during non-sleep resting states (Brokaw et al., 2016).

Recent studies reveal that resting-state functional connectivity can predict LTM retention differences, as observed in both EEG and fMRI research (Zhou et al., 2021; Xu et al., 2021). These studies also find a correlation between resting state and the rate of LTM forgetting, suggesting a biological basis for memory retention capabilities. Rate of forgetting, which serves as a good operationalization of LTM forgetting, is a valuable metric in memory process studies. It serves as a good predictor of how quickly information or skills are lost without active retention or practice (Sense et al., 2018).

Objective: Literature indicates that during resting states the brain has a different brain configuration. Since resting state is connected to consolidation, it would be expected to be reflected in the EEG signal. The objective of this study is to explore whether neural correlate can predict consolidation status of a memory trace. In other words, to test whether we can assess, using EEG measurements, if knowledge is “long-term stored” after an initial learning session. Additionally, utilizing resting-state functional connectivity alongside the rate of forgetting to enhance making this prediction.

EEG can already predict successful memory formation during learning which of the items would be remembered 24 hours later (Kang et al., 2020). They observed significant power spectrum differences in EEG signals when learning material was first presented and during task segments. Our goal is to find a neural marker, with the use of EEG, which makes it possible to discern whether a particular item has been categorized into long-term memory as a result of the learning process. Following this we will perform an exploratory analysis to see if there are potential differences in EEG signal for the items that individuals would versus would not be remembered several days later, exploring the possible neural differences for remembered and forgotten items.

Design/methods: This study involves a combination of behavioral testing and EEG analysis to investigate long-term memory consolidation. The experimental design is structured over a period of one workweek.

On Day 1 (n), participants will perform a MemoryLab studying session, in which they will be exposed to three blocks, each containing 20 items. The purpose of this session is to encode the memory items, setting the foundation for subsequent memory recall/EEG analysis.

The following day (n + 1), the studied items will be tested while measuring EEG to assess their recall of the studied words. This session will also include a period of restudy, allowing for re-encoding of the memory items. In addition, resting-state EEG data will be collected to analyze brain activity patterns when the participants are not actively engaged in a task. A second testing of the items will be conducted to reassess word recall following the resting state period, which will also be measured with EEG.

Three days later (n + 4), participants will complete a behavioral recall test to measure the retention of the studied words. This test will serve as a test to see if we can indeed predict whether something is consolidated days after the learning process.

Conclusion: The outcomes of this project have the potential to enhance our understanding of the neural mechanisms underlying long-term memory consolidation. If we can identify differences of long-term consolidation in the EEG signal, then there is a neural marker associated with memory retention and forgetting. This research could then pioneer new scientific insights into the neural basis in memory processing. Given that we would find something, it could support more targeted research into specific brain areas involved in the memory consolidation process. This might then contribute to optimizing learning strategies or help in the diagnosis and treatment of memory pathologies.

B2

Tackling Misfolded Protein Aggregation in Neurodegenerative Diseases: Development of a Super Chaperone

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Background Newly synthesized proteins are at risk of misfolding and aggregation, potentially leading to toxicity. To maintain the balance between folding and unfolding and prevent the toxic accumulation of misfolded proteins, the cells invested in a network of chaperones which promote efficient folding and ensure proper proteostasis. Recent findings suggest the involvement of deficiencies in the protein quality control and the proteostasis as the underlying reason for the manifestation and progression of neurodegenerative diseases that are indeed hallmarked by the progressive accumulation of protein aggregates (Hartl et al., 2011). Central to the maintenance of protein homeostasis are molecular chaperones of which the cells contain over 100 different ones. DNAJB6 is one of such chaperones that works in conjunction with heat shock proteins such as Hsp70 to maintain proteostasis. Several studies have shown that DNAJB6 is able to suppress protein aggregation both in vitro and in vivo settings (Kakkar et al., 2016 & Thiruvalluvan et al., 2020). Kakkar et al (2016) have generated mutations in the S/T rich region in DNAJB6 and demonstrated that this region is crucial for DNAJB6's ability to interact with polyglutamine (PolyQ) peptides to prevent their aggregation in vitro, a hallmark of CAG repeat expansion disorders such as Huntington's disease. Furthermore, they have shown that aggregate formation was reduced in DNAJB6 transgenic HTT (DNAJB6/HTT) mice expressing exon-1 of the human huntingtin gene and the motor dysfunction symptoms were delayed in DNAJB6/HTT transgenic mice compared to HTT mice. Moreover, DNAJB6 knockdown was shown to increase hypersensitivity to PolyQ aggregates in cultured cells derived from Huntington's disease patients, illustrating the importance of DNAJB6 against aggregation (Thiruvalluvan et al., 2020). All in all, these findings indicate the potential for targeting DNAJB6 in developing novel therapeutic strategies to address protein aggregation in neurodegenerative diseases.

Objective The main objective of the current project is to identify which mutational variants of DNAJB6 are more efficient in preventing the aggregation of varying lengths of polyglutamine (PolyQ) aggregates in vitro. Considering the use of the PolyQ aggregates, the focus of the project will be on Huntington's disease.

Design/methods A set of mutational variants of DNAJB6 will be generated and Human Embryonic Kidney 293 (HEK-293) cells will be transfected with plasmids carrying different mutational variants of DNAJB6. Obtaining mutations in the S/T rich region in DNAJB6 will be the main priority as this region has been implicated in PolyQ binding (Kakkar et al., 2016). The G/F region will also be investigated. If a mutational variant is found successful in preventing aggregation of PolyQ peptides, the mutational variant will then be tested for their efficiency in preventing the formation of PolyQ aggregates with different lengths.
Suppression of PolyQ aggregation by DNAJB6 will be analyzed using the filter-trap assay, automated live cell microscopy, western blotting, and immunofluorescence stainings.
PCR and qPCR will be carried out to investigate the gene expression and the mRNA levels of DNAJB6 in cells.

Conclusion Investigating the effects of mutations in specific domains of DNAJB6 to understand its role in preventing protein aggregation, could potentially lead to therapeutic approaches aimed at increasing its activity in aging cells to combat aggregation effectively.

C1

Vetoing the execution of hand movements through delayed presentation of potential new targets

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Keywords: readiness potential, movement vetoing, point of no return, internally-driven choice.

Background

The readiness potential (RP), observed in EEG, serves as the trigger that initiates a cascade of events in the brain that lead to the execution of a movement. This phase essentially represents the planning of a movement. Research in this field indicates that it is possible to interrupt this cascade of events initiated by the RP, effectively aborting a planned movement. A critical threshold, approximately 200 ms before movement execution, has been identified: beyond it avoidance of the movement becomes not possible. These findings hold significance for Brain-Computer Interfaces (BCI) as they address the challenge of determining when a subject decides to alter initial plans and refrain from executing a pre-planned action. However, the identification of the vetoing signal, the precise cause of interrupting the cascading events of the RP, and the possibility to detect this signal when the decision to avoid an action is subjectively driven (potentially involving higher cognitive demands) remain open questions.

Objective

The main objective of the planned project is to identify when a subject opts to alter the initial plan for executing a hand movement. Specifically, the goal is to identify when a distractor, presented later in comparison to the target, serves as a signal to veto the planned movement due to its higher perceived reward (defined either by the experimenter or the subject himself). The two main hypotheses are: 1) a more rewarding distractor, when compared to the target, leads to a change in plan and the vetoing of the movement; and 2) if the distractor is presented within a 200 ms timeframe before the movement's execution, the movement becomes unavoidable, even when the distractor is more rewarding.

Design/methods

The research revolves around collecting and analyzing data of an experiment in which participants are exposed to a target followed by a distractor, presented on a screen in front of them, with the possibility of the distractor leading to a change in the execution of the planned movement based on the subject's perception of reward. The methods that will be used for the data collection step are: EEG, EMG, EOG; for the data analysis: filtering, classification, linear discriminant analysis (LDA), independent component analysis (ICA).

Conclusion

The primary impact of the results from this project and related research in the field is the possibility to enhance neuro-prosthetic control. For example, if a subject, using, for instance, a prosthetic hand, decides to abort a movement after the planning procedure (and the related RP) has commenced, it is important to ensure that the robot hand does not execute that particular movement. Additionally, this project has the potential to provide insights into the impact of subjectively driven choices on the decision to abort planned movements (in case the target choice is internally-cued, i.e. chosen based on subjective preferences).

C2

Unravelling the Structure-Function Relation of the Chaperone DNAJB6b

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Background

Maintaining protein homeostasis in cells relies on the proper functioning of Protein Quality Control (PQC) systems which include molecular chaperones that interact with and stabilize proteins. DNAJB6b is a molecular chaperone which has been shown to play a crucial role in preventing aggregation of several disease-related intrinsically disordered proteins such as polyglutamine (polyQ), amyloid beta (Aβ) and alpha-synuclein (α-Syn). It is part of the heat shock protein network and it is known to interact with the Hsp70 system. Furthermore, certain mutations in DNAJB6b are linked to limb-girdle muscular dystrophy type D1 (LGMDD1). Recent all-atom molecular dynamics simulations showed that DNAJB6b is a transiently interconverting protein, cycling between three states: a *closed* state, an *open* state and a less frequent *extended* state. The extended state is hypothesized to be the functional state of the chaperone. However, in every state, including the extended state, an autoinhibitory anchor between helix V in the G/F_1 region and helices II/III of the J-domain, was observed which prevents Hsp70 from interacting with DNAJB6b's J-domain.

Objective

The aim of this project is to understand what relieves the autoinhibitory anchors observed in the molecular dynamics simulations which would allow DNAJB6b to interact with Hsp70 where this interaction has been shown to be important in preventing aggregation of several types of proteins. Our hypothesis is that the release of autoinhibition happens through the allosteric effects of a substrate binding to the domain rich in serine (S) and threonine (T) amino acid residues on the protein – the S/T domain. This is consistent with the hypothesis that the extended state is the functional state of the chaperone since in this state, DNAJB6b exhibits an exposed, extended S/T domain which would increase the probability of substrate binding to it. In this case, the substrate is hypothesized to include proteins with an expanded polyglutamine tract, associated with Huntington's disease since these are prone to forming β-sheet structures that contain β-hairpin motifs which are known to interact with the S/T domain.

Design/methods

In this project, we plan to use all-atom molecular dynamics simulations to probe the atomistic interactions between a single DNAJB6b protein and a single polyglutamine (polyQ) to test our hypothesis. For this, we will be using the GROMACS molecular dynamics package. We will examine these interactions when DNAJB6b starts in a closed, open and extended state. For each state, multiple simulations will be run with polyQ in a different position relative to DNAJB6b in order to better confirm the robustness and consistency of observed phenomena by sampling from a diverse set of initial conditions. Analysis will be performed on the data obtained from the simulations.

Outlook

Through this project, we endeavor to enhance our comprehension of the intricate functional properties of DNAJB6b through a detailed and mechanistic exploration of this molecular chaperone. The results from this project could inform future in vivo studies in this domain such as through cellular and animal models. Overall, this knowledge could contribute to the development of targeted interventions to mitigate protein aggregation-associated diseases.

D1

Sensory processing differences during development in genetic models of autism spectrum disorder

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Background: In up to 90% of individuals diagnosed with autism spectrum disorder (ASD) sensory abnormalities are reported, and among them, 60% specifically report tactile sensitivities (Tomchek and Dunn, 2007; Tavassoli et al., 2014). These symptoms are already present during early life (Estes et al., 2015). In mouse models for ASD, these behavioural deficits have also been found in a developmental time-dependent manner (Bruining et al., 2015). Additionally, sensory symptoms are highly correlated with other behavioural symptoms associated with ASD, such as social difficulties (O Miguel et al., 2017; Wiggins et al., 2009). Therefore, it might be possible that sensory deficits arise before behavioural deficits. However, there is still much to uncover on how the somatosensory system and social behaviour are related.

Objective: This project is based on previous findings and existing literature and work that show sensory differences in autism mouse models. The tests we propose here have already been performed in other mouse lines (Shank3 and Cntnap2) and have shown interesting results. Therefore, this project aims to further investigate sensory processing deficits as well as molecular mechanisms in the NRXN1 genetic ASD mouse model. NRXN1 knockout mice have been shown to exhibit behaviours relevant to these disorders, such as social interaction deficits and repetitive behaviours (Dachtler et al., 2015). Next to this, it has been shown that the heterozygous deletion of neurexins in mice led to dysregulation of the mTOR pathway, which may contribute to the observed behavioural deficits (Dachtler et al., 2015). As ASD is a developmental disorder, the behavioural tests will be done at three different developmental stages.

Methods: The NRXN1 animals will be assessed at three developmental time points: ±6 & 12 & 18 weeks.

Von Frey test
To test peripheral tactile sensitivity the von Frey test will be used. This test is specifically focused on hindpaw sensitivity by applying von Frey filaments of increasing or decreasing strength to both the left and right hind paws of the mice. Pressure is applied until the filament bends to ensure the right amount of pressure.

Tactile PPI
This test consists of giving the mouse acoustic startle pulses and smaller pre-pulse (air-puffs on their back) in different combinations over different trials. The response of the mice to the acoustic startle pulse will be recorded as a measure of the startle reflex. In addition, to measure PPI, different pre-pulses will be given before the onset of the startle pulses. Consequently, the ability of such a tactile pre-pulse to inhibit the startle response will be measured.

Potential impact: With the outcomes of this project, more knowledge can be gained on the genetics and molecular mechanisms that are involved in the sensory and behavioural differences observed in autistic people. The results of this project could identify new targets and time points in development for treatment strategies in autism spectrum disorders.

D2

Unravelling Synaptic Mysteries: White Matter Tracts and Synaptic Density in Patients with Schizophrenia Spectrum Disorder

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Background

Schizophrenia spectrum disorder (SSD) can be classified when a patient exhibits at least one of the following symptoms: delusions, hallucinations, or disorganised speech. SSD is thought to be caused by alterations in the brain, like excessive synaptic pruning. Brain tissue alterations can be investigated using PET- and DWI-scans.

PET-scans can visualise synaptic density using the [11C]UCB-J radioligand. This radioligand binds synaptic vesicle glycoprotein (SV2A), which is expressed in presynaptic vesicles of axon terminals. Multiple studies report lower synaptic density in SSD in multiple brain regions, aligning with post-mortem studies findings.

One measure of DWI is fractional anisotropy (FA), which may be a proxy of white matter deficits. Multiple studies report reduced FA in SSD in various brain regions, such as the temporal lobe. White matter deficits may proportionally increase from early-stage SSD to chronic SSD, with symptom severity correlating with the extent of white matter deficits

Objective

The objectives of this project are to analyse if there are differences in white matter tracts (between to be determined regions of interest) between patients with SSD and healthy controls using DWI measures. Furthermore, it is aimed to investigate in these regions of interest whether DWI measures correlate with synaptic density, as measured with PET-scans. Previous studies have shown evidence for a decrease in synaptic density as well as white matter deficits in patients with schizophrenia compared to healthy controls. Our hypothesis is that there will be similar results in this study, namely white matter deficits and a reduction in synaptic density.

Design/methods

In this project, PET-scans and DWI-scans of patients with SSD and healthy controls will be analysed to investigate the synaptic density and white matter tracts. The methods mostly comprise data analysis of PET- and DWI-scans that were previously made.

Conclusion

By gaining more knowledge on the synaptic density and white matter tracts in SSD compared to healthy controls, we are closer to identifying the processes that are different in SSD and potential therapeutic targets to ameliorate the symptoms in SSD.

E1

The role of sensory modalities in the interplay between social interactions and sleep in *Drosophila melanogaster*

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Background

Sleeping and social interactions are two widely conserved phenomenon, fundamental for the well-being of animals. These regulate essential homeostatic pathways crucial for normal brain function. *Drosophila melanogaster* is a model organism that is extensively used to study the interplay between sleep and social interactions. Studies have repeatedly showcased that sleep in fruit flies is modulated by social interactions. Recent unpublished data from the Billeter lab suggests that flies exposed to increasingly complex social environments for several days exhibit progressively higher sleep needs post-social grouping. To evaluate this further, they monitored sleep/rest rhythms and quantified social interactions in grouped flies over several days. This revealed that fruit flies exhibit enhanced social interactions during night, a period often associated with increased sleep; raising the question of whether they form groups not just for socializing but also for communal sleep. Given the potential evolutionary advantages of communal sleeping, it is important to understand if this phenomenon exists in fruit flies.

In this species, chemical communication is a key component of many group interactions and behaviour, emphasizing the importance of understanding sensory modalities in communal sleep and their impact at both the group and individual levels.

Objetive

The project aims to explore which sensory systems are involved in social interactions, in *Drosophila melanogaster,* and how variation in these abilities can impact sleep at the individual and group levels. First, we will focus on quantifying the occurrence and investigate the frequency of communal sleep; then on how group size influences the occurrence of communal sleep; and finally on the role of sensory modalities in communal sleep.

Design/methods

The project will use genetically modified Drosophila melanogaster for sensory systems. They will be set in groups, of different sizes, in arenas with food and video recorded for 4 to 5 days continuously. The video recording rig is constituted of a single-board computer Raspberry Pi and a system of 20 Raspberry Pi cameras, which allow to record 20 replicates experiments simultaneously. Bowl-shaped arenas will be used to ensure the right position of the flies for the cameras. The flies will be individually recognised and tracked by the open-source machine learning-based tool, Trex; which will be coupled with an in house python script to classifying behaviours essential for discerning social interactions and sleep patterns in fruit flies. The data will be processed with the Python script that processes the outputs from Trex to identify bouts of social interactions and sleep and finally quantify communal sleep.

Conclusion

Exploring the sensory systems involved in Drosophila melanogaster sleep enable a new approach to understand the interplay between social interactions and sleep. Because of the genetic tractability and the well-known neural circuits of Drosophila, this project could unravel the mechanisms of communal sleep and progress its evolutionary comprehension; giving insight into the benefit of group living in both Drosophila and other species.

E2

Understanding the relation between reward-cognition interactions and incomplete recovery of MDD: A Dynamic Functional Activity Study

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Background

Cognitive control is linked to fronto-parietal brain regions, including medial- and lateral prefrontal areas, lateral inferior parietal areas, the caudate nucleus, and the anterior mid-cingulate cortex (aMCC), which play a role in reward processing and proactive cognitive control allocation during goal-directed behavior (Duverne & Koechlin, 2017; Parro, 2018; Ridderinkhof et al., 2004). The aMCC, crucial for computing the expected value of cognitive control investment, integrates motivational signals (Shenhav et al., 2013). Reduced functioning in these regions is observed in Major Depressive Disorder (MDD; Van Tol et al., 2021), along with emotion regulation difficulties (Pico-Pérez et al., 2017). Individuals with remitted MDD (rMDD) struggle to engage fronto-parietal regions without clear task goals, yet demonstrate normal activation when explicitly instructed to solve complex problems. Suggesting that individuals with rMDD possess the ability to mobilize control resources but struggle in the absence of clearly defined task goals.

Objective

Investigating whether individual differences in how cognitive control is engaged have implications for functional recovery or the risk of relapse. The current study will investigate dynamic functional connectivity (dFC) between the striatum and anterior mid cingulate cortex (aMCC) using the Phase Synchronization method. We will:

1. Investigate whether the activation of cognitive control areas during tasks requiring sustained control is contingent upon interactions with reward-processing areas.
2. Examine and quantify the degree of interaction between cognitive control areas (aMCC) and reward-processing areas, specifically assessing whether this interaction is lower in individuals with remitted Major Depressive Disorder (rMDD) compared to those who have never experienced depression.

Design/methods

Phase Synchronization will assess dynamic network connectivity, focusing on synchronized oscillatory fMRI activity. Using the Parks-McLellan filter (McClellan et al., 1973) and Hilbert Transform, we'll analyze phase differences and calculate the Kuramotor Order parameter for quantifying synchronization degree (Acebrón et al., 2005; Kuramoto, 1984).

Conclusion

Understanding dFC during cognitive control tasks can provide insights into neurobiological mechanisms. Investigating whether individual differences in how cognitive control is engaged have implications for functional recovery or the risk of relapse.

F1

Activity-Silent (De)Coding of Retrieved Long-Term Memories

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Background
The understanding of working memory (WM) maintenance has shifted from a model solely based on sustained neural activation to one that includes both persistent activity and transient, activity-silent states. This model introduces short-term synaptic plasticity as a key mechanism that allows to temporarily represent information "silently", complementing maintenance via spiking neural activity. Information in such activity-silent states is accessed through state-dependent read-out, where a general stimulus prompts a specific response from the network, revealing the stored content due to residual synaptic activity. The research will build upon this foundational work, extending it to the realm of retrieved long-term memory (LTM) representation.

Objective
The project aims to investigate whether activity-silent states, initially identified in WM studies for the maintenance of new information, also apply to retrieved LTMs. A key hypothesis is that the retrieval of LTMs, involving cortical reactivation similar to initial memory encoding, might trigger short-term synaptic changes that lead to the representation of these memories in activity-silent states, paralleling the process observed with newly perceived information. The project further seeks to explore the interaction between new information and retrieved LTMs within these activity-silent states, hypothesizing that this interplay may influence memory updating and comparison of new and past information.

Design/methods
The project will employ the perturbation approach pioneered by Wolff et al. (2017), utilizing EEG to probe activity-silent states. This technique involves introducing a neutral impulse stimulus during a delay period and using EEG to decode the brain's response to this stimulus under various working memory (WM) conditions. The impulse stimulus helps in decoding activity-silent states by eliciting neural responses that reflect the synaptic activity associated with maintained memory content, even when it is not overtly detectable.
The method will be adapted to study the representation of retrieved LTMs in activity-silent states. This involves creating scenarios where subjects are exposed to cues to retrieve LTMs, followed by the presentation of the impulse stimulus to probe neural responses related to the retrieved LTM content.

Conclusion: The outcomes of this project will advance our understanding of how retrieved LTMs are represented and integrated with new information. By investigating LTMs representation via activity-silent states, this research has the potential to reshape theories of memory, offering insights into how past information interacts with ongoing perception and how long-term memories are updated to integrate new information.

F2

Unravelling Age-Related Changes in Vocal-Motor Control of Loudness in Zebra Finches

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Background

It is known that songbirds are a good model for studying vocal learning due to their neural similarities to humans regarding vocal learning pathways (Bolhuis and Moorman, 2015). The zebra finch (Taeniopygia guttata), a songbird, is widely used to study vocal learning.

Zebra finches can discriminate between songs and are capable of error correction which requires detection of subtle alterations and the precise control of distinct song features (Mol *et al*., 2021; Brainard, S., and Doupe, J., 2013; Sober, S. J., and Brainard, M. S., 2009). Therefore, zebra finches are suitable models for understanding vocal-motor control of loudness (Badwal, A., *et al*., 2020).

Age affects many body functions which is also verifiable in zebra finches. It is known that age affects the vocal-motor control in zebra finches (James, S., and Sakata, T., 2014; Badwal, A., *et al*., 2020). The detection of errors in a song and their consequent correction seems to be affected by ageing (Badwal, A., *et al*., 2020). However, to understand the connection between ageing and vocal-motor control of loudness further research is needed.

Objective

Control and speech production is a complex topic and can be impacted by ageing or certain diseases. Those aspects are valid not only in humans but also in songbirds with the last ones providing crucial insights to human therapies. The project aims to characterise the impact of age on neural control of vocal loudness in zebra finches. Ultimately, the characterisation provides a better understanding of the neural mechanisms behind vocal-motor control of loudness in zebra finches through different periods of their lives.

Design/methods

Zebra finches at younger and older ages will be tested in an altered auditory feedback setup. This setup is composed of two speakers placed as earphones and a microphone. Through the speakers, zebra finches will hear their own songs with alterations in real-time. However, prior to that, I will participate in the calibration of the sound intensity and build our own database of songs.

Conclusion

A better understanding of the neural mechanisms behind vocal-motor control of loudness in zebra finches is crucial. A better knowledge of the normal loss that occurs with ageing can give clues to how motor diseases impair vocal learning. Especially since after understanding the normal mechanism, models of some diseases in zebra finches can be accessed to compare and understand better the affected mechanisms.

This project will ultimately contribute to a better understanding of vocal-motor control loss with ageing, possibly leading to improvements in the speech rehabilitation area.

G1

Exploring the influence of Cognitive Reserve as a protective factor for Alzheimer's disease: A multi-method approach

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Background Given the current Alzheimer's epidemic, with an estimated 32 million people worldwide suffering from the disease, and projections indicating a doubling of these numbers within the next two decades, the imperative for research in early detection and intervention and possible protection becomes evident.[1,2] It is known that cognitive reserve (CR), the brain's capacity to offset the effects of age-related cognitive decline, can serve as a protective factor to Alzheimer's disease.[3,4] CR is a complex construct, with facets ranging from social lifestyle to educational activities and from hobbies to linguistic abilities: because of this, there is ongoing debate about the best way to measure CR and what factors significantly contribute to CR.[5] It is known that bilingualism positively contributes to CR, and lifelong bilingualism may delay the onset of Alzheimer's Disease with approximately 4 years.[6,7] The study aims to investigate the interplay of factors that contribute to the build-up of CR in middle adulthood. This research combines neural patterns by means of EEG/fNIRS, genetic predisposition to Alzheimer's Disease and measures of cognitive reserve.

Objective The main objective of the project is to investigate whether a significant role of cognitive reserve can be identified by means of resting-state EEG and fNIRS profiles and in middle-aged adults with and without a genetic predisposition for Alzheimer's Disease. The hypothesis is that distinctive neural patterns during rest will be evident in individuals with varying levels of cognitive reserve. The research into the relation between cognitive reserve, a genetic predisposition for Alzheimer's disease and neural patterns takes different cognitive reserve related lifestyles into account, specifically but not limited to linguistic behaviors. This way, we aim to map the brain's ability to withstand damage and neural patterns during rest and through that formulate a research agenda for further research in this promising area. This exploration could be of high relevance in terms of early detection of Alzheimer's Disease, as well as the potential for delaying the onset and identifying protective factors and hence possibly preventive strategies to improve cognitive reserve in middle-aged adults.

Design/methods The current project, part of the G-LEAP project (Genetics, Language Experiences and Aging Project), consists of a comprehensive battery of assessments that combines cognitive tests, questionnaires, and neurophysiological measures (specifically EEG and fNIRS). Data is collected during two sessions with participants between the ages of 45 and 65. Participant sessions consist of an initial online screening, along with language tests, and are followed by a practical session where participants complete tests while EEG/fNIRS data is being collected. This session incorporates a neurocognitive test battery, including eyes-open and eyes-closed resting-state EEG/fNIRS recordings, cognitive tasks (Stroop Arrows, Color-Shape Switching), and a working-memory task (Digit Span), and two language tasks (Semantic Verbal Fluency task in Dutch and a Semi-structured Interview). The task that will be a focus point in the current study is the Cognitive Reserve Scale (CRS).[8] These data will be connected to subjects' genetic predisposition to Alzheimer's Disease and resting-state EEG and fNIRS data.

Conclusion The project outcomes could provide valuable insights into risk factors and protective factors for Alzheimer's disease and the influence of cognitive reserve. Moreover, for potential (pre-clinical) diagnostic purposes of Alzheimer's disease, it is important that specific neural patterns are identifiable. Research into the build-up of CR, especially in middle adulthood, could provide valuable insights into maximizing the cognitive reserve and potentially delaying the onset of Alzheimer's Disease or cognitive decline. Exploring distinctive neural patterns in at-risk middle-aged adults may contribute to research relating to early detection strategies and the crucial roles of cognitive reserve and language in clinically diagnosing and preventing Alzheimer's Disease.

G2

Can tTIS Modulate Oscillations in Deep Brain Structures to Influence Emotion Processing?

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Background
Emotion processing is a fundamental cognitive ability, for which the amygdala is a key brain region. However, there are currently no approved non-invasive techniques to focally stimulate deep brain structures. Transcranial temporal interference stimulation (tTIS) is a novel technique which aims to solve this. While animal studies have shown its ability to modulate neural activity in focal, deep brain structures, human studies remain limited.

Objective
Therefore, the aim of the current study is to further validate the use of tTIS by examining its ability to modulate human brain oscillations in the amygdala and evaluating its subsequent impact on emotion processing.

Design/methods
Healthy first year RuG psychology students recruited from SONA will be randomly assigned into a sham or tTIS condition. Resting state magnetoencephalography (MEG) will be used to measure brain activity, then tTIS targeted to the amygdala or sham will start, followed by another MEG measurement and giving participants an emotion processing test.

Results
It is hypothesized that tTIS will result in significant changes in brain oscillations in the amygdala. It is further hypothesized that the tTIS condition will perform significantly better than the sham condition on the emotion processing test.

Conclusion
This study will allow for further validation of tTIS, which would make it possible to initiate research and clinical trials with patient populations in the future. Eventually, this could lead to an effective and non-invasive alternative treatment option for individuals who suffer from Parkinson's disease, dystonia, tremors, epilepsy, obsessive-compulsive disorder, treatment resistant depression, and tinnitus.

Keywords: temporal interference stimulation (tTIS), non-invasive brain stimulation, deep brain stimulation, neural modulation, emotion processing

H1

Extracting Intrasaccadic Electrophysiological Responses to Perceptual Input

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Background

In textbooks, we usually read that visual input during saccadic eye movements is largely ignored due to saccadic suppression. However, intrasaccadic input may be perceived when accounting for post-saccadic masking. Strikingly, contrast sensitivity during the saccade was even found to be comparable to fixation conditions when stimulus velocity was matched to saccade velocity. So far, those studies have relied on psychophysical tasks because of the large artifacts of saccadic eye movements on electrophysiological measures. However, new ICA-based techniques make it possible to correct for the influence of saccades. A promising approach that might provide a way to assess the influence of intrasaccadic input on the electrophysiological signal is the VESPA technique.
Using VESPA, visual evoked potentials were efficiently established in significantly less time than earlier approaches, employing random luminance modulations of stimuli frame by frame. However, those experiments only involved static viewing conditions. Combining this technique with the use of high-speed projectors may provide a route to investigate signatures of the intrasaccadic perceptual input in the EEG signal.

Objective

High frame rate projectors allow for presenting numerous contrast changes in the saccadic interval. Employing ICA-based correction techniques, we aim to eliminate signal artifacts caused by eye movements. Our goal is to integrate these approaches to examine electrophysiological data for evidence of perceptual influence. Offering a promising avenue to explore understudied intrasaccadic visual processing using electrophysiological measures.

Design/methods

The experiment comprises randomly mixing fixation and saccade trials. Saccade trials involve a jumping fixation point, while in fixation trials, participants gaze at the screen center. Background noise is bandpass filtered, and its contrast is modulated. EEG will be recorded for 15 participants across supervised sessions lasting about two hours. Analysis will include cross-correlations, temporal response functions, EEG preprocessing with EEGLAB, and eye movement data analysis by the student.

Conclusion

The findings could offer crucial insights into intrasaccadic perception using electrophysiological methods. Additionally, our approach may serve as a valuable means to assess sensory and perceptual processing, particularly in clinical subpopulations like autism and schizophrenia, shedding light on the effects of intrasaccadic perception on visual stability in these groups.

H2

Mechanisms of PRG5 signaling and protein quality control

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Background Plasticity-Related Gene 5 (PRG5) is a protein that presents a vertebrate-specific and neuronal-enriched pattern of mRNA expression [1], [2], [4], [5]. PRG5 expression is observed to be higher during CNS development, peak around the time of birth, and to be lower during adult stages [2], [3]. Only in areas of high synaptic plasticity and where adult neurogenesis can occur does PRG5 expression remain elevated [2], [4]. Additionally, its dynamic expression pattern during CNS development [5] along with an epileptic phenotype under KO conditions [6], highlights its developmental significance. Similarly, in vitro [2] and in vivo [5] studies show that PRG5 overexpression increases dendritic spine density and PRG5 inhibition reduces dendritic spine density, this highlights PRG5's necessity for and capability of PRG5 for spinogenesis. PRG5 is a member of the Lipid Phosphate Phosphatase (LPPs) superfamily that comprises integral membrane glycoprotein enzymes, which all contain six transmembrane domains with three extracellular loops containing one conserved ectophosphatase site, that are involved in the regulation of extracellular concentration and signal transduction of lipids, such as Lysophosphatidic Acid (LPA) and Sphingosine-1-Phosphate (S1P), by catalyzing their dephosphorylation [7]. Analytically, in the Plasticity-Related Gene (PRG) subfamily the residues responsible for ectophosphatase activity are modified, thus rendering PRG5 without enzymatic activity [5]. However, even without this catalytic activity, PRG5 still affects LPA signaling since overexpression of PRG5 attenuates neurite retraction induced by LPA [4].
PRG5-induced protrusion formation is independent of the conventional Cdc42/mDia1 pathway [4], and whether it involves PRG5 interacting with bioactive lipids or other yet to be identified factors remains a mystery.

Objective/Goal The purpose of the project is to identify the factors that are involved in the formation of plasma membrane protrusions, mediated by PRG5.

Design/Methods Initially, we will utilize mass spectroscopy to determine possible molecules that interact with PRG5 within protein lysates obtained from mouse cortex, cerebellum and hippocampus after immunoprecipitation of PRG5 [8]. Subsequently, we will validate these obtained "hits" through biochemical methods and we will explore their role in the induction of morphological changes along with their dependence on PRG5. Additionally, we will perform a screen for the pathways involved in the induction of morphology changes by using pharmacological inhibitors that target major signaling molecules and kinases such as cyclic AMP (cAMP), protein kinase A (PKA) and small GTPases. Specifically, in order to perform the aforementioned, we have established a Flp-In™ T-Rex™ HEK293H cell line that expresses eGFP-tagged PRG5 under a Tet-inducible promoter (Tet-On System). Induction of PRG5 overexpression will lead to morphological changes and we will assess the effect of the pharmacological compound on these morphological changes. Finally, upon identification of inhibitors inducing morphological alterations, we will use the interactome data to determine which factors govern the pathways identified in the screen and we will link the interactors discovered in our initial proteomic analysis with pathways that include the factors affected by the effective inhibitors.

Conclusion Overall, this project will help us identify a major signaling pathway underlying brain plasticity. Because spine abnormalities are found in many pathological conditions, including mental illnesses and age-related neurodegenerative diseases [5], PRG5 levels might be relevant for the susceptibility, pathophysiology, or therapy for such diseases [2]. Specifically, description of this signaling pathway will also help identify additional possible targets suitable for pharmacological intervention [2].

I1

Exploring Ferroptosis in Tauopathies: Paving New Paths for Parkinsonism Treatment

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Background Ferroptosis represents a distinct mode of non-apoptotic cell death, delineated by iron-catalyzed lipid peroxidation processes (1). Iron is an indispensable component of cellular function due to its pivotal role in numerous metabolic pathways (2). Consequently, cells employ intricate iron homeostasis mechanisms (3). However, in ageing and age-related diseases such as parkinsonism, these mechanisms tend to become dysfunctional (4). The exploration of ferroptosis thus emerges as a potential therapeutic avenue in these conditions. Ageing has been linked with the progressive impairment of protein quality control mechanisms (5), predisposing individuals to an escalated risk of pathological protein aggregates. Among these are Tau protein inclusions, characteristic of atypical parkinsonian syndromes such as Progressive Supranuclear Palsy (PSP) and CorticoBasal Degeneration (CBD). Although the ferroptosis pathway has been linked to Parkinson's Disease pathology (6-8) and iron accumulation in the substantia nigra (SN) has been linked to PD progression (9), the specific role of ferroptosis in atypical parkinsonism remains underexplored. This gap in knowledge further motivates our proposed investigation into the interplay between tauopathies in parkinsonism and ferroptotic processes. This further motivates the current proposal on finding the relationship between tauopathies in parkinsonism and ferroptosis. However, whether the pathology is a cause or consequence of ferroptosis in the progression of parkinsonism, remains an open question.

Objectives 1a. Study the interaction of hyperphosphorylated tau and ferroptosis: evaluate mRNA expression profiles of ferroptosis-related genes in post-mortem parkinsonism human SN neurons with and without tau inclusions, using the nanoString GeoMX Digital Spatial Profiler. 1b. Evaluate viability and ferroptosis marker expression of LUHMES dopaminergic neurons after addition of tau protofibrils. 1c. Intervene in this process by knock-down/pharmacological manipulation of ferroptosis-related markers: pharmacologically stimulate/inhibit ferroptosis in LUHMES dopaminergic neurons with tau toxicity and evaluate cell viability and network formation. 2a. Evaluate expressions patterns of 6 ferroptosis related markers in the noradrenergic Locus coeruleus and compare these results with previous data obtained from SN.

Methods Digital Spatial Profiling (nanoString GeoMX)
From the SN of a mixed cohort of 10 PSP/CBD patients, and 10 age-matched controls a Tissue Micro Array (TMA) block was constructed. A paraffin TMA section will be double immunolabelled using anti-Tau (AT8) and anti-Tyrosine Hydroxylase. As the focus of the study are dopaminergic neurons, the TH-tag allows for isolation of these cells (i.e. no glia, etc). In addition, the section will be hybridised with gene-specific probes towards all protein-coding mRNA transcripts in the tissue. Apart from ferroptosis-related transcripts we plan to perform pathway analysis as well to generate new hypotheses.
LUHMES cell culture are dopaminergic cells seen to be vulnerable to ferroptosis (10). These cells will be cultured in 96-well plates with tau-protofibrils, a toxic species of tau used in vitro. Besides routine cell viability assays, the cells will also be studied for detection of lipid peroxidation; as a positive control, Erastin and/or RLS3 will be used to induce ferroptosis. These experiments will answer the question to what extent tau can induce ferroptosis. In a second series of experiments, ferroptosis (induced by either tau or pharmacological drug) will be inhibited using Ferrostatin, ALOX-inhibitors and Deferoxamine. These experiments will help understand whether tau-induced ferroptosis can be inhibited with these different drugs and which one is more efficient.

Conclusion/Impact Analysis of the ferroptosis pathway in vitro and in vivo will help understand the relationship between ferroptosis and tau in the progression of PSP/CBD. It is our hope that the findings of this research will reveal novel therapeutic avenues for slowing down/stopping parkinsonism progression.

I2

Perinatal Fluoxe.ne Exposure Affects the Myelin-Related Gene Expression of Juvenile Rats

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Background

According to the World Health Organization, about 10% of pregnant women worldwide suffer from depression and they are mostly treated with selec3ve serotonin reuptake inhibitor (SSRI) antidepressant intake. Both human and animal studies have shown that there are long-term and sex-specific alterations caused by *in utero* SSRI exposure. Ramsteijn et al., (2022)[1] showed that perinatal fluoxe3ne (SSRI) exposure enhanced myelin-related gene expression in the prefrontal cortex (PFC) and inhibited it in the basolateral amygdala (BLA) and such effects were stronger in males than in females. Myelina3on is a crucial process in brain development. In rodents, it is underway by postnatal day (PND) 10-14 and peaks at PND 202, with the limbic system as one of the last regions to be fully myelinated[1].

Objective

It is suggested that perinatal exposure to SSRIs accelerates brain maturation, with the peak of BLA myelination happening before PND 21 (hence, the decrease) and the peak of PFC myelina3on happening around PND 21 (hence, the increase)[1].
The objective is to establish the myelin-related gene expression at different time points (PND 2, 7, 14, 21, 35, and 70) to check whether brain maturation is accelerated under perinatal fluoxetine exposure. I will be investigating the myelin expression on PND 21.

Design/methods

Firstly, the animal work concerning the fluoxetine administration and brain dissection had to be done. Then, the 200 µm brain slices will be created using cryostat for a subsequent tissue punching of PFC and BLA. Further, the RNA isolation, cDNA preparation, and qPCR will be performed for specific myelin-related genes (*Mag* and *Mbp*).
There is a possibility of an extension to other genes or brain areas if time allows.

Conclusion

As around 10% of pregnant women worldwide suffer from depression, it is crucial to assess what are the effects of antidepressant treatment on the development of the baby. Current studies do not provide appropriate informa3on on this matter. The potential outcomes of the project may provide significant insight into the effects of perinatal SSRI exposure on the offspring's neurodevelopment.

J1

The Effects of Artificial Light at Night on Sleep, Physiology and Behaviour of Rats

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Background To navigate the daily challenges posed by environmental light-dark conditions, various life forms have evolved light-responsive systems, extending beyond visual experiences and influencing critical physiological and behavioural aspects. Light photons interact with photopigments in retinal photoreceptor cells, transmitting signals to retinal ganglion cells that convey information to diverse brain centres. Thereby, light influences physiology and behaviour via two primary pathways; by synchronising and modulating the endogenous biological clock, and by directly affecting brain centres responsible for tuning physiology and behaviour. While light at the right time is crucial for performance and well-being, improper light timing, as seen with artificial light at night (ALAN), can disturb typical sleep architecture and ultimately lead to health detriments. Research reveals that subtle changes in light intensities at night alter sleep and affect activity patterns. Moreover, some animals exhibit sensitivity to light cues, with levels as low as 0.05 lux inducing circadian activity shifts. This sensitivity suggests that minimal levels of ALAN could mask natural cues and induce physiological changes. Sleep deprivation results in lower levels of the Brain-Derived Neurotrophic Factor (BDNF). BDNF plays a crucial role in neuronal and synaptic plasticity and is therefore widely implicated in psychiatric diseases.9 Yet, the extent to ALAN effects on sleep, physiology and BDNF levels remain largely unknown across species.

Objective The present project aims to investigate the effects of ALAN on the physiology and behaviour of the nocturnal rat. The following subgoals are proposed: 1) To Determine what the effect of ALAN is on sleep architecture and quality. 2) To determine if the effects of ALAN depend on the intensity of light. 3) Compare the effects of acute vs. chronic ALAN exposure. 4) To determine what the effect of ALAN is on BDNF levels. We hypothesise that ALAN will significantly disrupt physiology and behaviour in rats, for the different objective we composed the following hypothesis: ALAN will result in atypical sleep architecture, and poorer sleep quality of the rats, which will be light intensity-dependent. Prolonged exposure to ALAN will increasingly disrupt sleep architecture and activity patterns of rats in time. Latstly, poor sleep quality as a result of chronic ALAN exposure will lead to decreased BDNF levels.

Design/methods Before the start of the experiments, surgeries will be performed on the rats for implanting intraperitoneal thermal loggers and EEG/EMG & brain thermal electrodes. A housing system will be installed for rats, which will include controllable lights and passive infrared tracking system. Instead of a standard 12:12 LD cycle (baseline), during the experimental night the animals will be exposed to artificial light with intensities ranging from 0 - 100 lux. After establishing the acute effect of ALAN we will investigate changes in similar parameters during chronic exposure to ALAN. Brain activity, brain temperature and movement will be recorded via the EEG dataloggers. The acquired data will be analysed for various parameters such as sleep consolidation, length, power spectra and composition of different sleep stages. EEG data will be scored with automated scoring program *Somnivore* and further analysed in R and/or other suitable programs. Additionally, urine and blood will be sampled during different experimental conditions to measure BDNF levels and other metabolites of the rats.

Conclusion Light pollution and irregular lighting conditions pose significant challenges in society and ecosystems. Studies show that ALAN may cause detrimental health effects, including circadian disruption, cardiovascular deficits, sleep disorders, and increased risk of cancer in humans. This project aims to explore how ALAN affects physiology and behaviour in rats. Understanding the disruptive effects of ALAN is crucial for grasping the broader ecological implications and developing strategies to reduce its adverse consequences on wildlife and human health. In addition, this project aims to unravel the relationship between ALAN and BDNF, which will not only enhance understanding on this topic but also provides valuable insights translatable to human psychiatric studies. Insights may inform workplace regulations, targeted treatments for light-related pathologies, and guidelines for healthy light exposure.

J2

Rat sexual and aggression behaviour in response to an SSRI and 5-HT1A-antagonist

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Background

Selective serotonin reuptake inhibitors (SSRI's) are often prescribed for people suffering from depression. However, the effects of SSRI's on behaviour are poorly understood. Though some studies suggest SSRI's have no effect on aggression [1], other studies suggest a there is an effect [2]. One of the ways in which this may be caused is that SSRI's lead to apathy, resulting in violence [3]. As of yet, studies concerning the use of SSRIs and occurrence of aggression show conflicting results. Similar confusion exists around the effect of SSRI's on sexual behaviour. Though it is generally believed SSRI's reduce sexual behaviour [4], there are also cases in which it is believed to cause hypersexuality [5]. Both aggression and arousal are regulated by the same brain region, and perhaps this could play a role in the conflicting results that are found on the effect of SSRI's on both aggression and sexual behaviour [6]. The topic requires further research, to clarify the role of serotonin in behaviour and the potential downsides of using SSRI's to combat depression.

Objective

The objective of the study is to see whether or not a SSRI causes aggression and enhances sexual behaviour. To measure the acute effects the SSRI will be given in combination with a 5-HT1A-antagonist. This is tested by injecting rats with a 5-HT1A-antagonist and a SSRI. Before and after this, aggressive behaviour and sexual behaviour will be tested.
It is expected that the SSRI and 5-HT1A-antagonist will increase both aggressive behaviour and sexual behaviour, in accordance to reportings from humans [2, 5].

Design/methods

During this project sexual behaviour and aggression will be tested with Observer XT. Aggressive behaviour will be tested by the resident-intruder test. Sexual behaviour will be tested weekly by a 30-minute sex test.
Following this, pharmacology will be carried out in which injections will be given with fluoxetine and a 5-HT1A-antagonist. Following this, aggression and sexual behaviour will be tested again.

Conclusion

Studying the effect of SSRI's on aggression and sexual behaviour is important for our understanding on the effects of serotonin as neurotransmitter. Furthermore, understanding the effects of these medications is important in case these medicines are administered, since experiencing alterations in behaviour caused by their medicine may lead to stress or disrupt quality of live.

K1

Testing LGMD mutation regarding aggregating and degradation myotilin

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Background

Limb-girdle muscular dystrophy (LGMD) is a autosomal dominant muscle disorder, characterized by myofibrillar degeneration, autophagic vacuolation and aggregation of myofibrillar proteins (M. Abayev-Avraham et al., 2023, A.R. Findlay et al., 2023). Research has indicated that dominant forms of LGMD are caused by mutation in DNAJB6, an HSP40 co-chaperone that facilitates HSP70 functionality through its J domain (A.R. Findlay et al., 2023, H. H. Kampinga & E. A. Craig, 2010). The DNAJB6 is a co-chaperone that is part of the heat chock proteins and is involved in a wide range of cellular events, including protein folding (He, Y. & Z. Wang. 2022. Individuals with Limb-Girdle Muscular Dystrophy (LGMD) have been identified with specific mutations in DNAJB6, with F100V being one of them; however, the precise impact of these mutations on cellular functions remains unclear (L. Masino et al., 2011, C. de Chiara et al., 2013).The goal of this research is to investigate is to explore how LGMD-associated DNAJB6 mutation F100V affects aggregation and degradation of Myotillin, another muscle-associated protein.

Objective

The purpose of this study is to investigate the effects of the LGMD-associated DNAJB6 mutation F100V on the aggregation and degradation of Myotillin. The hypothesis is that a mutation of the F100V gene will affect functionality of DNAJB6 towards the substrate processing , but this effect will mostly be observed upon application of heat shock. According to M. Abayev-Avraham et al. (2023), disease mutants of DNAJB6 were still as effective as the wildtype protein at preventing amyloid aggregation, but they did structural differences in the J-domain which might indicate a disruption of regulation of DNAJB6-Hsp70 binding. It is expected that a difference in functionality of the DNAJB6 towards the Myotillin processing will be observed when heat shock is added as a stressor because the DNAJ co-chaperone belongs to family of heat chock proteins.

Design/methods

Initially, HEK293 cells will be used in cell culture experiments, along with transfection to introduce the mutant DNAJB6 and the Myotillin. Afterwards, methods for protein isolation and fractionation will be employed to extract the protein in various forms, including soluble forms, gel-like structures, and aggregates. Western blotting is used after protein extraction to identify and measure the protein in various states. The blot image analysis will be performed using ImageJ software. Furthermore, the mutant protein stability will be explored both in the absence and presence of the substrate.

Conclusion/Impact of outcomes

The outcomes of this research project have important implications for understanding and possibly modulating the progression of the limb-girdle muscular dystrophy (LGMD) associated with the DNAJB6 mutation F100V. Should the research indicate an effect on protein turnover, it may pave the way for personalized lifestyle modifications and thereby personalized treatment with the aim of influencing the progression of the disease. For example, this could involve strategies to reduce stressors on muscle proteins and thereby improve overall protein. As patient differences should be taken into account, such interventions may not only help slow down the progression of the disease but also lay the foundation for personalized therapeutic approaches.

K2

Antithrombotic medication in acute ischemic stroke patients with tandem lesion: subgroup analysis of MR CLEAN MED.

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Research project of the UMCG neurology department, using the data of the MR CLEAN MED TRIAL

Background

Around 20% of people who had an acute ischemic stroke in the anterior circulation also have a tandem lesion. This consists of an intracranial occlusion with a stenosis or an occlusion in the ipsilateral extracranial carotid artery. The treatment of a tandem lesions is challenging; Treating with IV thrombolysis leads to good clinical outcomes in only 17% of cases with a death rate as high as 55% (Papanagiotou et al., 2011). The HERMES meta-analysis of tandem lesions patients demonstrated that EVT is more beneficial than using IVT alone (Papanagiotou et al., 2018). The optimal treatment for the extracranial carotid artery lesions has yet to be defined. There is however mounting evidence that emergent stent placement in the carotid artery could lead to better recanalization rates and improved clinical outcomes(Farooqui et al., 2023) (Zhu et al., 2019). However, evidence is still lacking regarding the optimal antithrombotic regimen during immediate stenting. With carotid artery stenting there is a balance between the risk of second intracerebral haemorrhage (sICH) and the risk of in-stent thrombosis. An aggressive regimen increases the risk of sICH and a less aggressive treatment increases the risk of in-stent thrombosis.

Objective

Using the data from the MR-CLEAN MED TRIAL the differences in functional outcome on the modified Rankin scale at 90 days will be analysed between patients with immediate carotid artery stenting and patients who underwent EVT without carotid artery stenting.
Subquestions:

- What are the differences between the heparin and aspirin group?
- What is the difference between patients receiving thrombolysis and patients without thrombolysis.

Design/methods

The data of the MR CLEAN MED trial will be used for this research. In the MR CLEAN MED trial patients were randomized to receive aspirin, heparin, both or neither. The analyses will be performed in R. Figuring out how to analyse the data and how to use R will be part of the project.
The data is not accessible yet, after the data has been viewed the methods that will be used will be further determined.

Conclusion/Impact of outcomes

The outcomes of this project will be part of a larger research project determining the best way to treat acute ischemic stroke in tandem lesion patients. The outcomes of the larger research project will adapt the guideline regarding the treatment of patients with tandem lesions.

L1

Exploring the Role of SPP1-Expressing Microglia: Altered Interactions with Central Nervous System Cell Types in Alzheimer's Disease

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Background

Alzheimer's disease (AD), affecting 35 million globally yearly, is a major cause of dementia.
Characterized by amyloid-β aggregation and tau hyperphosphorylation, its underlying disease mechanism remains elusive. Recent research highlights microglia's crucial role in disease progression. Microglia, essential for the brain's immune response, also contribute to neuronal support and synaptic organization[1]. Interestingly, in AD microglia exhibit an altered phenotype[2].
The presence of this altered phenotype to humans was previously unknown. Recent research of this group identified distinct microglial genetic profiles associated with amyloid-β plaques (AD1) and tau pathology (AD2) suggesting altered microglia phenotypes in humans3. SPP1, upregulated in AD1 microglia[3], is intriguing for its role in microglial-neuronal interactions. Previous studies link SPP1 in damaged cells to increased cognitive decline, implicating the SPP1 microglia in synaptic protein engulfment and pro-inflammatory phenotypes in AD mice4. However, SPP1 upregulation in AD1 microglia is associated with a phagocytic/activated microglia phenotype3, which could potentially be protective by aiding in plaque clearance.

Objective

Upregulation of SPP1 protein and its presence in AD1 microglia could thus aid in the clearance of ab or could be detrimental to disease progression by potentially accelerating cognitive decline through the engulfment of seemingly intact synapses.
Thus, this project aims to confirm the presence of the SPP1 expression in AD1 microglia in AD postmortem brains. Furthermore, the localization of SPP1-expressing microglia and its interaction with CNS cells will be explored.

Design/methods

Immunostaining of postmortem human AD brains is a key method, involving tissue processing and cryostat sample cutting. To facilitate this, commercially available SPP1 antibodies will be used to detect SPP1-expressing microglia. Additionally, we will determine which cell types are predicted to have altered SPP1 signaling from microglia, and similarly use antibodies for receptors of SPP1.
Data analysis will be conducted, utilizing microscopy for visualizing immunostained brain tissue sections and image acquisition techniques for quantifying protein expression levels, assessing cellular distribution, and comparing neuronal networks between samples.

Conclusion

This project aims to advance our understanding of Alzheimer's disease by investigating the role of SPP1-expressing microglia in amyloidosis. Confirming SPP1 upregulation in postmortem human AD brains could provide crucial insights into neuroinflammation and cognitive decline mechanisms.
Characterizing the presence and impact of SPP1-expressing microglia at a cellular and molecular level, offers the potential for targeted therapeutic interventions in Alzheimer's disease.

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