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ANNUAL MEMBERS' DAY

2026

Theme Influencing the Brain: how thoughts and feelings are shaped by actions and experiences

Location UMCG, Hal 3219/Anda Kerkhoven Centre 0103

Date Time 6 February 2026
09:00 - 17:00

Poster Presentations PhD-students / ReMa-students Program

- 09:00 – 09:30** **Registration with coffee/tea**
- 09:30 – 09:55 Welcome by BCN board
- 09:55 – 10:00 PhD Council
- 10:00 – 10:15 **BCN Lecture FSE:** Suzanne van der Veldt
Sex differences in anxiety: what the rodent brain can tell us
- 10:15 – 10:30 **BCN Lecture FL:** Ellie Harding
Music: resonating in the brain and culture
- 10:30 – 11:10** **Coffee/tea break**
- 11:10 – 11:15 Gathering groups
- 11:15 – 12:15 Poster Presentation (PhD candidates & ReMa students group sessions)
- 12:15 – 13:15** **Lunch + free poster session**
- 13:15 – 13:30 **BCN Lecture BSS:** Marieke Pijnenborg
Can Social Media Rot Your Brain?
- 13:30 – 13:45 **BCN Lecture FW:** Daphne Brandenburg
Liberalism for Brains That Can't Help Themselves
- 13:45 – 14:00 **BCN Lecture UMCG:** Marc van Dijk
Access to the Brain
- 14:00 – 14:15 Presentation Seed Grant winners
- 14:15 – 14:30 Presentation Winner BCN Dissertation Award
- 14:30 – 15:00** **Coffee/tea break**
- 15:00 – 16:00 Influencing the Brain – Science writing for a general audience
- 16:00 – 16:25 Meet the BCN Board
- 16:25 – 16:35 Awarding of BCN Poster Awards
- 16:35 – 17:00** **Drinks**

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Poster Groups PhD-students

Group 1 (gathering at board no. 1)

1. Tim van Brouwershaven
2. Xiaolin Zhu
3. Yadong Liu
4. Lina Albakri

Group 2 (gathering at board no. 5)

5. Anna Straatsma
6. Eline Bosch
7. Marlies Oegema
8. Nursena Ataseven

Group 3 (gathering at board no. 9)

9. Francesca Borghese
10. Bandana Mainali
11. Jente Zeubring
12. Mirthe Ronde

Group 4 (gathering at board no. 13)

13. Esmée Dragt
14. Wieke de Jager
15. Ge Li
16. Sidra Jendo

Group 5 (gathering at board no. 17)

17. Osman Oguz
18. Changxiao Kuai
19. Tina Drincic
20. Kim Hurst

Group 6 (gathering at board no. 21)

21. Doreen Oosterhoff
22. Marie - Christine van de Glind
23. Eva Geerts
24. Qiwen Tang

Group 7 (gathering at board no. 25)

25. Veera Ruuskanen
26. Manon Werst
27. Zhenyu Zhang
28. Caitlin Grieve

Group 8 (gathering at board no. 29)

29. Luisa Epifani
30. Kateryna Skupovska
31. Jiahao Li
32. Karina Köpke

Group 9 (gathering at board no. 33)

33. Almut Jebens
34. Irene de Nijs
35. Taku Otsuka
36. Jo-Anne van der Sluijs

Group 10 (gathering at board no. 37)

37. Dora van Elk
38. Maria João Caiado
39. Parisa Nobari
40. Hui Ling Li

Group 11 (gathering at board no. 41)

41. Mirjam van Tellingen
42. Iris Hamers
43. Nienke Buist
44. Özde Sönmez

Group 12 (gathering at board no. 45)

45. Giulia Mozzanica
46. Tamara Hageman
47. Floor Gelmers
48. Amber Woudstra

Poster Groups Research Master-students

Posterboard nos. A1 – V1

Group A (Suzanne van der Veldt – evaluator) (*gathering at board no. A1*)

A1	Ilse Bakker
A2	Kim Barbara
B1	Nikola Bátorová
B2	Jan Bethe
C1	Audry Bos
C2	Merlijn Brouwer
D1	Julia Burgos Flores

Group B (Sanne Moorman - evaluator) (*gathering at board no. D2*)

D2	Simone Cidoni
E1	Lene de Jong
E2	Suzanne Lunshof
F1	Nastasia Drgalová
F2	Inge Eisberg
G1	Tellos Fatta
G2	Javier Garrido Jiménez

Group C (Guillaume Etter - evaluator) (*gathering at board no. H1*)

H1	Manousos Vitzilaios
H2	Hidde Huisjes
I1	Ilaria Iele
I2	Jasper Wannet
J1	Amber Kal
J2	Vasileios Kapantaidakis
K1	Emily Kenneally O'Donohoe

Group D (Defne Abur - evaluator) (*gathering at board no. K2*)

K2	Mariëlle Kuipers
L1	Saga Lehtimäki
L2	Giorgia Marrone
M1	Linda De Pellegrin
M2	Li-Yan Sijbolts
N1	Marysia Michalak
N2	Maria Ogîrcin

Group E (Mark Nieuwenstein - evaluator) (*gathering at board no. O1*)

O1	Hanna Sieka
O2	Thijs Peters
P1	Marta Prati
P2	Başak Saraçoğlu
Q1	Jenny Sauerbier
Q2	Fiete Schmitt
R1	Moniek Schulting

Group E (Martien Kas - evaluator) (*gathering at board no. R1*)

R2	Laura-Marie Oldörp
S1	Indy Lopers
S2	Iarina Şimon
T1	Livia Stein
T2	Anna Stróżyk
U1	Wies van der Hout
U2	Paula Gomez Mendez
V1	Sara Jugănaru

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Relationship between anticholinergic burden, symptomatology, functioning, quality of life, and recovery in psychosis: a network analysis

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⁵UMC Utrecht, Department of Neuroscience, Utrecht

⁶KieN VIP Mental Health Care Services, Department of Research and Innovation, Leeuwarden

Background

Many psychotropic medications used to treat psychiatric symptoms or to manage side effects have anticholinergic properties. The use of multiple anticholinergic agents, or anticholinergic burden, is negatively correlated with several cognitive domains in people with Schizophrenia Spectrum Disorders (SSD). The exact role that anticholinergic burden plays in the interrelationships between cognition, negative symptoms and functioning, and how anticholinergic burden may be related to quality of life and recovery in individuals with SSD remains unclear.

Objective

To examine the (in)direct relationships between anticholinergic burden, symptomatology, functioning, quality of life, and recovery in people with SSD in a network-analysis.

Design/methods

Data was obtained from the Pharmacotherapy Monitoring Outcome Survey study for adults with a psychotic disorder. Anticholinergic burden was assessed with the Anticholinergic Burden Scale; positive, negative, and cognitive symptoms were measured using the Positive and Negative Syndrome Scale; global functioning was assessed with the Health of the Nation Outcome Scales, and the WHO Disability Assessment Schedule; quality of life was assessed with the Manchester Short Assessment of quality of life, and the EQ-5D. We used a partial correlation network analysis to assess associations between anticholinergic burden, symptoms, cognition, global functioning, and quality of life. Additionally, a stricter model which reduced the number of associations to those that were most robust was analysed.

Results

The total sample consisted of 1090 individuals. Anticholinergic burden was directly connected with the two negative symptom domains social amotivation and expressive deficits, cognition, and antipsychotic dose. Anticholinergic burden was indirectly associated with daily functioning and quality of life via negative symptoms and cognition. In the stricter model, anticholinergic burden was only associated with antipsychotic dose.

Conclusion

Our results suggest a unique association between anticholinergic burden and different symptomatic domains. Anticholinergic burden seems, at least to some extent, interact with negative symptoms and cognitive impairment. Rather than focusing on anticholinergic burden in isolation, the results highlight the importance of addressing the broader constellation of clinical and functional domains that shape outcomes in individuals with SSD.

Deciphering the Cellular Heterogeneity of Familial Frontotemporal Dementia

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Isabelle Le Ber², Morwena Latouche², Renee van Buuren³, Susanne Kooistra¹,
John C. van Swieten³, Bart J.L. Eggen¹

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³ Department of Neurology & Alzheimer Center, Erasmus University Medical Center, Rotterdam.

Background

Frontotemporal dementia (FTD), the second most prevalent form of dementia, is characterized by progressive behavior and/or language impairment and mainly affects the frontal and temporal lobes of the neocortex. Approximately 30% of the FTD cases has a genetic etiology. Mutations in the progranulin gene (*GRN*) or the chromosome 9 open reading frame 72 gene (*C9orf72*) are two major causes of genetic FTD.

Objective

While a substantial number of studies focused on neuronal changes in human FTD, other cell types in central nervous system, including glial cells, may also influence progression of the disease. With this study, we aim to delineate the cellular heterogeneity of these cell populations in FTD-GRN and FTD-C9 and identify disease-associated changes.

Design/methods

We collected frozen human brain tissue from Netherlands Brain Bank in Amsterdam and NeuroCEB brain bank in Paris. We included affected regions (frontal cortex, temporal cortex, thalamus) and a non-affected region (occipital cortex) from FTD-GRN donors, FTD-C9 donors and control donors. Tissue blocks were cut into sections for nuclei isolation. NeuN^{neg}Oligo2^{neg} nuclei were collected using fluorescence-activated nucleus sorting (FANS) to exclude neurons and oligodendrocytes and enrich for less abundant cell types. The collected nuclei were loaded on a 10X single nucleus sequencing platform (snRNAseq). Tissue stainings of pathological markers and potentially relevant proteins were performed to confirm pathology and validate snRNAseq data.

Results

We identified disease-associated microglia in affected regions in both FTD-GRN and FTD-C9 cases. Two clusters of astrocytes with high expression of WDR49 also showed enrichment in disease affected regions. In contrast to what was previously described for FTD-GRN, the neurovascular unit was unaffected in FTD-C9.

Conclusion

Overall, our results indicate that although driven by two different mutations, there could be shared mechanisms and affected cell types in FTD-GRN and FTD-C9. Further analyses are ongoing and could provide insights for target finding and therapy development for FTD patients.

Parietal Regional Homogeneity Predicts Recovery Outcomes in Older Patients with Mild Traumatic Brain Injury

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*Corresponding authors

Background

Older patients with mild traumatic brain injury (mTBI) have heightened risk for incomplete recovery, yet prognostic neural markers remain poorly defined.

Objective

We investigated whether brain regional homogeneity (ReHo), a measure of local neural synchrony, can function as mTBI-related neural marker and predict symptom burden and functional recovery.

Design/methods

Twenty-five older mTBI patients (>60 years) and 20 age-matched controls underwent resting-state fMRI one-month post-injury (3T). Voxel-wise ReHo was computed using CONN toolbox. Group differences and whole-brain correlations between ReHo and severity of injury-related complaints (determined with the Head Injury Symptom Checklist) were assessed ($p < 0.001$ uncorrected, cluster FDR $p < 0.05$). Functional recovery was assessed using the Glasgow Outcome Scale Extended (GOSE). Identified cluster ReHo was correlated with 3-month symptoms and compared between CR (GOSE=8) vs. IR (GOSE<8) groups using permutation tests.

Results

Patients showed increased frontal and decreased sensorimotor ReHo. Whole-brain correlation identified a right superior parietal lobule (SPL) cluster negatively associated with concurrent complaints ($r = -0.81$, $p < 0.0001$), depression ($r = -0.65$, $p = 0.0002$), and anxiety ($r = -0.58$, $p = 0.002$). One-month SPL ReHo was associated with 3-month symptom severity (complaints: $r = -0.57$, $p = 0.004$; depression: $r = -0.48$, $p = 0.018$; anxiety: $r = -0.44$, $p = 0.033$). IR patients had significantly lower ReHo in sensorimotor regions at 6 months ($p = 0.012$, $r = 0.62$) and SPL at both 3 months ($p = 0.028$, $r = 0.54$) and 6 months ($p = 0.033$, $r = 0.53$).

Conclusion

Desynchronization in sensorimotor and SPL emerge as a potential prognostic marker. Although parietal ReHo showed no group differences, its strong outcome association suggests individual neural reserve variation. Decreased SPL ReHo predicts persistent symptom burden and incomplete functional recovery, suggesting that parietal integrity determines individual vulnerability to poor outcomes and support risk stratification for targeted intervention.

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Tinnitus: an underreported condition following microvascular decompression for hemifacial spasm

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Background

While hearing loss is a well-known condition following microvascular decompression (MVD) for hemifacial spasm (HFS), tinnitus is an underreported one.

Objective

This study aims to identify prevalence, characteristics, severity, and predictors of tinnitus following MVD for HFS.

Design/methods

A single-center cohort of 55 HFS patients completed a questionnaire approximately 5 years following MVD. Data encompassed tinnitus presence, side, type, onset, and severity measured by a 10-point Visual Analogue Scale (VAS). Descriptive, correlation, and logistic regression analyses were conducted.

Results

At surgery, participants' median age was 58 years (IQR 52–65). The median duration of HFS symptoms before surgery was 5 years (IQR 3–8), slightly predominant on the left (60%). Postoperative tinnitus was reported by 20 patients (36%), versus nine (16%) that reported preoperative tinnitus. Postoperative tinnitus was ipsilateral on the surgical side in 13 patients (65%), bilateral in six (30%), and contralateral in one (5%). Among patients with bilateral postoperative tinnitus, 33% did not have this preoperatively. Tinnitus was continuous in 70% of cases and pulsatile in 30%. Onset of new tinnitus was in 58% immediately or within days, in 25% within three months, and in 17% between three months and one year after surgery. The mean severity of postoperative tinnitus was 5.1 points on the VAS. Preoperative tinnitus and presence of arachnoid adhesions had suggestive associations with postoperative tinnitus in initial analyses ($p=0.005$ and $p=0.065$). However, preoperative tinnitus was the only significant predictor of postoperative tinnitus ($p=0.011$).

Conclusion

Tinnitus is a common condition following MVD for HFS, with a moderate overall severity. Causes behind postoperative tinnitus remain obscure but could be related to those of postoperative hearing loss in this patient population. Clinicians should be aware of tinnitus following MVD and vigilantly monitor its occurrence, to facilitate prevention efforts and optimize outcome for HFS patients undergoing MVD.

Examining Heterogeneity in the Mild Traumatic Brain Injury Population: A Latent Class Analysis of Subacute Symptoms and Associations with Long-Term Outcomes

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Background

After mild traumatic brain injury (mTBI), there is substantial heterogeneity in both symptom presentations and long-term outcomes. Many patients have suboptimal long-term outcomes after mTBI. To facilitate early and individualized care for these patients, it is important to examine whether and how specific combinations of symptoms are associated with poor long-term outcomes.

Objective

In the present study, we examined whether clusters of patients with mTBI with similar posttraumatic complaints and psychological characteristics could be identified. We also examined the 6-month outcomes and demographic and clinical characteristics of the clusters.

Design/methods

In an observational cohort study, 653 patients with mTBI completed measures of posttraumatic symptoms (cognitive, sleep, fatigue, pain, vestibular and somatic symptoms) and psychological characteristics (depression, anxiety, posttraumatic stress, passive coping, self-efficacy) at 2 weeks post-injury. Latent class analysis was performed to identify distinct clusters of patients. The identified clusters were related to outcome measures obtained at 6 months post-injury: functional recovery, quality of life and return to work.

Results

Nine clusters of patients were identified. Clusters not only differed in their overall levels of symptom burden and psychological characteristics, they also demonstrated distinct symptom profiles. The clusters showed differences on all 6-month outcome measures. Clusters with better functioning at 2 weeks post-injury generally demonstrated more favorable 6-month outcomes. Clusters with good functioning at 2 weeks after mTBI generally consisted of relatively more men than clusters with poor functioning, where the sex distribution was more equal. There were also differences between clusters for level of education, premorbid mental health problems, presence of CT abnormalities, injury severity and day-of-injury alcohol use, but no clear pattern emerged regarding the associations of these variables with functioning at 2 weeks or outcomes at 6 months.

Conclusion

The present study shows that distinct symptom profiles can be identified early after mTBI based on questionnaire data. Such early and comprehensive assessment of patients' symptoms and psychological characteristics offers insight into the 6-month outcomes of the clusters. Furthermore, our results support the notion that different groups of patients with mTBI have different symptoms and thus require different treatment approaches, highlighting the need for individually tailored care in this patient population.

Sex differences in antidepressant serum levels

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Background

Antidepressants are among the most widely prescribed drugs worldwide, with use more than twice as high in women as in men. Sex influences antidepressant pharmacokinetics, potentially leading to sex differences in antidepressant tolerability, safety and therapeutic response, yet current prescription guidelines account for sex. This study investigated sex-related differences in serum levels of 11 commonly prescribed antidepressants, including SSRIs, SNRIs, TCAs, NaSSAs.

Objective

To determine whether sex is associated with systematic differences in antidepressant serum levels in a real-world clinical population, and to evaluate whether such differences warrant consideration in future sex-informed dosing recommendations.

Design/methods

Serum levels of amitriptyline, nortriptyline, citalopram, clomipramine, fluoxetine, fluvoxamine, imipramine, mirtazapine, paroxetine, sertraline, and venlafaxine, along with their active metabolites, were collected from the laboratory information system (GLIMS) database of the University Medical Centre Groningen between January 2016 and October 2024. When metabolites exhibited comparable pharmacological potency, parent and metabolite concentrations were summed. Linear mixed-effects models were applied. The dataset comprised 38,298 samples from 10,500 unique adult men and women. To assess whether dosing differences contributed to the sex differences in serum levels, subgroup analysis using dosing data from the MONitoring psychoPHARmacology (MOPHAR) program was performed.

Results

Women exhibited significantly higher serum levels than men for citalopram (+38%, $p < 0.001$), fluoxetine (+20%, $p = 0.002$), fluvoxamine (+85%, $p < 0.001$), paroxetine (+51%, $p < 0.001$), sertraline (+13%, $p = 0.048$), clomipramine (+10%, $p < 0.001$), imipramine (+20%, $p = 0.001$), nortriptyline (+9%, $p < 0.001$), and venlafaxine (+25%, $p < 0.001$). Trend level higher serum levels were observed in women for amitriptyline ($p = 0.058$). Dosing did not significantly differ between sexes, except for higher doses in men than in women for clomipramine ($p = 0.016$) and nortriptyline ($p < 0.001$).

Conclusion

Under current treatment guidelines, women are exposed to significantly higher antidepressant serum levels than men for five of the five SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline), three of the four TCAs (clomipramine, imipramine and nortriptyline), and the SNRI venlafaxine, despite uniform dosing recommendations. Subgroup analyses indicated that dosing was unlikely to have caused the observed sex differences. Whereas SSRI, SNRI, and NaSSA are prescribed using standardized dosing regimens, TCA dosing is guided by therapeutic drug monitoring (TDM). The smaller, though persisting, sex differences observed for TCAs suggest that TDM partially mitigates but does not fully eliminate sex-related pharmacokinetic variability. These findings underscore the importance of considering sex in antidepressant dosing strategies for women using antidepressants, with the goal of optimizing treatment effectiveness, tolerability, and safety.

Phonological, morphological and syntactic features in mild, moderate and severe Alzheimer's disease – A systematic review

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Background: Despite previous systematic and scoping reviews addressing phonological, morphological and syntactic aspects in Alzheimer's Disease (AD), including broader or composite metrics and verb processing, a comprehensive overview of rule-based phonological, morphological, and syntactic features that characterize the mild, moderate, and severe stages of AD, both in comparison with cognitively healthy controls and across disease stages, is lacking.

Objective: To identify which phonological, morphological, and syntactic features in verbal (spoken) language production and comprehension characterize the mild, moderate, and severe stages of Alzheimer's disease.

Method: APA PsycINFO, CINAHL, EMBASE, LLBA, and PubMed/Medline databases were searched from inception to October 2024. Two researchers independently identified, screened and evaluated the methodological quality of the included studies following PRISMA-guidelines. The search combined AD-related terms with phonological, morphological, and syntactic keywords.

Results: In total, 39 studies were included: phonology (n = 5), morphology (n = 10), syntax (n = 18) and both morphology and syntax (n = 6). Most studies focused more on language production than language comprehension and were of moderate methodological quality. Phonological impairments became more diverse with increasing AD severity. Morphological deficits were reported; for mild AD, pronoun use. For mild, mild–moderate, and moderate stages, outcomes for verb and noun inflection were mixed. Comprehension deficits involved quantifier–mass/count noun agreement. Syntactic deficits occurred from mild to moderate-severe stages, especially at sentence and clause level.

Conclusion: The findings indicate a progressive deterioration of phonological, morphological and syntactic features across AD stages. Syntactic impairments were the most consistent at the sentence and clause level, followed by morphological deficits in verb inflection and pronoun use. Phonological impairments remain relatively preserved at mild stages. These features may help differentiate AD from healthy aging and between AD disease stages. Future research should apply longitudinal research, more precise staging methods and integrate multiple language domains to capture deterioration patterns.

Predictability stabilizes and reshapes the neural code.

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²: Ergonomics, Leibniz Research Center for Working Environment and Human Factors

Background

The human brain generates internal models to predict incoming sensory information and constantly updates these internal models based on experience (Clark, 2013, 2015; Friston, 2005, 2010). Perception and cognition do not simply reflect incoming sensory information, instead it shows an integration of incoming information and generated predictions (Friston, 2005, 2010; Körding & Wolpert, 2004; Lee & Mumford, 2003; Rao & Ballard, 1999).

Objective

In this study, we aimed to conduct an in-depth investigation of how predictability alters neural representations. For this, we conducted a series of multivariate analyses on the neural variance and structural geometry of the same stimuli either when they are or aren't predicted.

Design/methods

Forty participants judged whether a probe grating was rotated clockwise or counterclockwise relative to a memorized orientation which was either predictable or unpredictable. Each memory item was preceded by a central color cue (red, green, or blue); two of these colors (predictive) cued two non-overlapping 90° segments of orientations that the item was sampled from in half of the trials; in the other half, a third (non-predictive) color was presented that signaled the item could have any possible orientation.

Results

Predictable items lead to better behavioral performance with systematic biases towards prediction templates. Orientations for both predictable and unpredictable items were similarly decodable from the EEG data during memory encoding. However, cross-condition decoding was significantly weaker than within-condition decoding, suggesting that the encoding format changed between conditions. Representational similarity analysis showed higher similarity between predictable items, with a representational bias towards the cued segment. Covariance matrices showed lower variance for predictable items while the representational space of predictable items was shrunk. These effects were absent during the maintenance phase.

Conclusion

Together, our findings suggest that diffuse predictions reshape neural representations and stabilize the neural code during encoding.

Light intensity modulates thermoregulation in a cooling environment

Borghese, F.¹ & Hut, R.A.¹

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Background

The suprachiasmatic nucleus (SCN), which receives its main input from light¹, is the pacemaker of the circadian system and regulates daily changes in physiological variables, including thermoregulation^{2,3}. Thermoregulation maintains temperature homeostasis through a balance of heat production and heat dissipation⁴ and its coordinating center, the hypothalamic preoptic area (POA), receives input from the environment as well as from the SCN to trigger appropriate thermoregulatory responses⁵. Across the day, core temperature follows a circadian rhythm, reaching its lowest point in the early morning and its peak in the evening⁶. Evidence suggests that exposure to bright light attenuates these SCN-dependent fluctuations⁷⁻⁹. While such effects are well established for nighttime bright light exposure, findings remain inconclusive when light exposure occurs during daytime^{8,10}.

Objective

We aimed to provide further insights into the effect of daytime light exposure on thermoregulation by measuring responses to changes in ambient temperature (increases or decreases) during the day while participants were exposed to dim or bright light.

Design/methods

24 participants took part in two experimental sessions: one in dim light condition (14 lux) and the other in bright light (5350 lux). They were placed in rooms set at 15°C, 25°C or 35°C, spending 30 minutes at each temperature before switching to another. The order of exposure to the different ambient temperature followed either a warming protocol (exposure to 15°C, then 25°C, then 35°C) or a cooling protocol (exposure to 35°C, then 25°C, then 15°C). Measurements of core and skin temperature were performed using swallowable telemetric sensors and temperature loggers respectively.

Results

After 20 minutes of exposure to each ambient temperature condition, we observed higher core temperature and lower peripheral temperature at 15°C, with the opposite pattern at 35°C, regardless of light condition. At 15°C, core temperature was lower in bright light compared to dim light, however, this effect was observed in the cooling protocol only.

Conclusion

These findings suggest that during daytime and in a cooling environment, dim light promotes better heat conservation than bright light.

Prevalence and Risk Factors of Dizziness as a Proxy for Vestibular Loss: A Lifelines Cohort Study

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Background

The vestibular system is essential for balance, spatial orientation, and coordination of eye and head movements. Loss of vestibular function can cause a heterogeneous range of disabling symptoms, commonly including dizziness, vertigo, unsteadiness, fall, affecting up to 30% of adults during their lifetime, with prevalence increasing with age. Vestibular loss (VL) has been associated with comorbidities such as cardiovascular disease, diabetes, hypertension, mental health disorders, hearing loss. Despite its high prevalence, up to 80% of VL cases are incorrectly and insufficiently managed. Identifying socio-demographic, clinical, and lifestyle factors associated with VL may improve understanding and develop effective prevention and management strategies. The Lifelines cohort provides a unique opportunity to investigate the prevalence of VL and its associated risk factors at a population level.

Objective

To estimate the prevalence of dizziness and its variation across sociodemographic group, and to identify associated socio-demographic, clinical, lifestyle risk factors.

Design/methods

This cross-sectional study used baseline data from the Lifelines cohort. Adults aged ≥ 18 years with available dizziness data were included ($N = 147,588$). Self-reported dizziness from questionnaires served as a proxy for VL. Data on socio-demographic, clinical, lifestyle variables were obtained through questionnaires, physical examinations, and laboratory assessments. Prevalence was estimated via descriptive analysis, and associations with potential risk factors were assessed using logistic regression adjusted for age, age², and sex, followed by multivariable modelling.

Results

Dizziness was prevalent in 18% of participants and was more prevalent in females than males (21.7% vs. 12.2%, $p < 0.001$). Although prevalence varies by age, no significant increasing trend with age was observed. Multivariable analyses are ongoing to identify independent risk factors associated with dizziness.

Conclusion

Dizziness is common in the general population and shows notable sex differences. This study provides population-based prevalence estimates and investigates underlying risk factors for dizziness.

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What has eye colour to do with CoA metabolism? Investigating pantetheine as a therapeutic candidate for the neurodegenerative disease PKAN

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Background

Pantothenate Kinase Associated Neurodegeneration (PKAN) is a recessive genetic disorder caused by mutations in Pantothenate Kinase 2 (PANK2), leading to brain iron accumulation and symptoms such as parkinsonism and dystonia, ultimately resulting in early death. PANK2 is involved in the first enzymatic step of Coenzyme A (CoA) biosynthesis from vitamin B5. Our lab aims to explore whether vitamin-B5 independent routes to CoA, like via pantetheine, can rescue PKAN models. Interestingly, we discovered that pantetheine works protective against PKAN, however, it also induces toxicity. The mechanisms causing this toxicity are unknown. We found that the eye colour mutant *white* in *Drosophila melanogaster* is hypersensitive for pantetheine, suggesting that this gene, which is coding for an ABC transporter, could play a role in pantetheine-dependent CoA metabolism.

Objective

We investigate the metabolism of pantetheine in relation to the *white* gene, aiming to optimise treatment for PKAN and gain new insights into CoA metabolism.

Design/methods

To model PKAN, we make use of the fruit fly *Drosophila melanogaster*. We add increasing doses of pantetheine to their diet and test different mutant fly lines to assess the toxic effects of pantetheine through a phenotypic survival assay. Flies that are sensitive to pantetheine die at larval stages, preventing their development into pupae or adults, allowing for the tally of surviving progeny. Additionally, fluorescent microscopy is used to find the localisation of the *white* gene and its interactors, as well as to elucidate their function in relation to pantetheine.

Results

White needs other members of the ABC transporter family to form a fully functioning transporter, such as *Scarlet*. Also, *scarlet* mutants exhibit toxicity to pantetheine as well. Using the UAS-GAL4 system, we show that knocking down *White* or *Scarlet* in the Malpighian tubules (equivalent to the fly kidney) resulted in pantetheine toxicity. Using mutant lines *White::GFP* and *Scarlet::GFP*, we confirmed the transporter's localisation in these tubules. Additionally, both the *White* and *Scarlet* proteins are found in vesicles that colocalise with lysotracker, identifying these vesicles as lysosomal-related organelles (LROs).

Conclusion

Pantetheine can rescue a PKAN fly model but causes toxicity in *white* or *scarlet* mutants. With targeted knockdown of *white* or *scarlet* in the Malpighian tubules, toxicity persists. Suggesting a role of the *White-Scarlet* transporter in Malpighian tubules in pantetheine metabolism. Lysotracker staining indicates that the *white-scarlet* transporter is located in LROs, yet the function of pantetheine related to these LROs is still unknown.

Default mode network dynamics and early social dysfunction in transgenic Alzheimer's mice

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Background

Social dysfunction is a core symptom across multiple brain disorders and emerges before overt pathology. The PRISM2 consortium identified and replicated that social dysfunction is transdiagnostically linked to reduced Default Mode Network (DMN) connectivity. These findings indicate that aberrant DMN dynamics may underlie shared social impairments.

Objective

To back-translate and further our understanding of this transdiagnostic relationship, we investigated social behaviour and network-level electroencephalographic (EEG) activity and connectivity in the 3xTg mouse model of Alzheimer's disease at a pre-pathological age.

Design

Young adult triple-transgenic (3xTg) and non-transgenic (NTg) mice of both sexes were subjected to two complementary social paradigms: (1) a semi-naturalistic social colony setup enabling longitudinal monitoring of social behaviour, and (2) the three-chamber test assessing acute sociability. Wireless depth EEG recordings were obtained from DMN-related brain regions in freely moving mice, and event-locked connectivity analyses (wPLI, dPLI) were used to study network dynamics during social behaviour. Absent amyloid pathology was confirmed by 6E10 immunohistochemistry.

Results

While overall levels of social interaction during longitudinal recording were often comparable between groups, differences emerged depending on the specific type of social behaviour and the phase of the day. In particular, 3xTg males tended to display more sustained social engagement than NTg controls during the active period, suggesting subtle alterations in social dynamics. Social behavioural features were closely linked to general locomotion, and substantial inter-individual variability was evident. Throughout acute social testing, group differences were more readily apparent, with 3xTg mice showing higher sociability than controls, an effect that was most pronounced in females.

Conclusion

These findings suggest that early-stage 3xTg mice display altered social dynamics prior to Alzheimer-like pathology, indicating that social changes may precede classical disease markers and extend beyond categorical diagnostic boundaries. The variability in all four groups suggests that early social changes indeed extend beyond categorical boundaries. Combining naturalistic and structured behavioural assays enhances translational relevance, while ongoing EEG analyses will clarify how early DMN alterations relate to these behavioural shifts and inform the development of transdiagnostic biomarkers.

Predicting relevant microglia-associated cell-cell communication pathways in Alzheimer's disease: a role for SPP1

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Background

Microglia, the innate immune cells of the central nervous system (CNS) parenchyma, play a significant role in the pathogenesis of Alzheimer's disease (AD). We previously identified two microglia transcriptomic states associated with amyloid-beta and tau pathology using single-nucleus RNA sequencing (snRNAseq) of control and AD brain tissue samples.

Objective

These AD-associated microglia states are expected to react and communicate differently with neighboring cells in the AD CNS. While our original study provided insights into microglial heterogeneity during disease progression, it was limited to neuron- and oligodendrocyte-depleted data.

Design and results

Here, we generated a complementary snRNAseq dataset from neuron- and oligodendrocyte-enriched unsorted CNS cells from the same control and AD brain samples. We explored alterations in microglial cell-cell communication pathways using CellChat to predict ligand-receptor-mediated interactions. This bioinformatic analysis predicted enriched SPP1 signaling by and to microglia in AD donors. We confirmed increased SPP1 expression in microglia using RNA-scope, where we observed that SPP1-expressing microglia were in proximity to amyloid-beta plaques. To assess if there is an effect of osteopontin, the protein product of *SPP1*, we performed a phagocytosis assay with human induced pluripotent stem cell-derived microglia-like cells (iMGLs). We observed that pre-treatment with recombinant osteopontin resulted in increased phagocytosis of pHRhodo-conjugated E coli particles by iMGLs.

Conclusion

These data imply that SPP1 is potentially a relevant cell-cell signaling molecule in the pathophysiology of AD.

Brain Injury Recovery after Symptom-guided Early Therapy (BRAIN-RESET) study protocol for a multicenter randomized controlled clinical trial

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Background

Mild traumatic brain injury (mTBI) is one of the most frequent neurological conditions in the Netherlands and a leading cause of long-term disability. Although prognosis is relatively favorable, over 70% of patients experience persistent post-traumatic complaints six months after injury, negatively affecting daily functioning, return to work or study, and quality of life. In the chronic phase, post-traumatic complaints are considered therapy resistant and no evidence-based treatment is currently available. Therefore, early intervention in the (sub)acute phase may prevent persistence of symptoms to improve functional outcome and quality of life.

Objective

The primary objective of this study is to improve early care for patients suffering from post-traumatic complaints after mTBI by developing and evaluating effective symptom-guided tailored interventions, as current care is limited to a wait-and-see policy in the absence of effective evidence-based treatment.

Study design

BRAIN-RESET is a prospective three-arm multicenter open randomized controlled trial (RCT). Adult patients aged 18-70 years diagnosed with mTBI at the emergency department of participating hospitals within 24 hours after injury will be eligible for inclusion. At two weeks post-injury, post-traumatic complaints will be assessed using the Rivermead Post-concussion Symptoms Questionnaire (RPQ). Patients meeting a predefined symptom threshold will be randomized between symptom-targeted therapy (physical and/or occupational therapy), psycho-education by telephonic counselling, and care as usual. Each patient will be followed for six months to assess the efficacy and sustainability of the intervention(s). BRAIN-RESET will be conducted in 8 hospitals in the Netherlands. A total of 655 patients will be included and randomized.

Study outcomes

The primary outcome measure will be the total RPQ sum score at three months post-injury. Secondary outcomes include post-traumatic complaints (RPQ) at six months post-injury, and functional outcome, cost-effectiveness, and quality of life at three and six months post-injury.

Summary

This randomized controlled trial will evaluate whether early, symptom-guided interventions can reduce post-traumatic complaints after mTBI. The study is expected to provide important insights into the feasibility and potential effectiveness of early targeted treatment, and to inform future implementation aimed at improving recovery and reducing long-term individual and societal burden.

PARP Inhibition Attenuates Neuroinflammation and Demyelination in a Mouse Model of Multiple Sclerosis: A [¹¹C]PBR28 TSPO PET Imaging Study

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Background

Neuroinflammation, driven by activated microglia, plays a key role in CNS disorders like multiple sclerosis (MS). PARP inhibition has been suggested to help reduce neuroinflammation and protect cellular integrity. PET imaging with the TSPO ligand [¹¹C]PBR28 allows in vivo assessment of glial activation.

Objective

Here, we explored the effect of PARP inhibition on neuroinflammation in vitro, and in a lysolecithin-induced MS rat model using PET.

Design/methods

In vitro, [¹¹C]PBR28 uptake was assessed in LPS-stimulated RAW264.7 macrophages in the presence or absence of the PARP inhibitor PJ34. In vivo, focal demyelination was induced in male Sprague-Dawley rats by unilateral lysolecithin injection into the corpus callosum and striatum. Animals received PJ34 (20 mg/kg, i.p.) or vehicle and PET imaging with [¹¹C]PBR28 was performed on day 3 and 7 post-lesion induction. Microglial activation and myelin integrity were confirmed postmortem by IBA-1 and Luxol Fast Blue staining.

Results

LPS stimulation (100 ng/mL) significantly increased in vitro [¹¹C]PBR28 uptake in RAW264.7 macrophages (1.9 ± 0.18 fold, $p < 0.0001$). PJ34 co-treatment (1 μ M) significantly reduced this increase in uptake to 1.2 ± 0.22 fold ($p < 0.0001$), indicating PARP inhibition attenuated LPS-induced macrophage activation in vitro. [¹¹C]PBR28 PET imaging revealed significantly lower tracer uptake in MS lesions in animals that were administered PJ34, compared to vehicle-treated controls on day 3 (SUVmean 1.21 ± 0.03 vs. 1.75 ± 0.04 , $p < 0.001$) and day 7 (SUVmean 1.00 ± 0.03 vs. 1.29 ± 0.06 , $p < 0.001$). In contrast, contralateral brain regions showed no differences in tracer uptake between treatment groups or between time points (SUVmean ~ 0.50). Immunohistochemistry confirmed a significant reduction in IBA-1 staining of microglia in PJ34-treated animals compared to vehicle controls. Luxol Fast Blue staining revealed a smaller demyelinated area in the PJ34-treated group, compared to controls, suggesting that PJ34 effectively attenuates demyelination.

Conclusion

This study demonstrates that PJ34 treatment can attenuate microglial activation and reduce demyelination in an MS model, supporting the hypothesis that PARP inhibition may have a neuroprotective effect in neuroinflammation-driven diseases.

Early Motor Development of infants born to mothers with Phenylketonuria: Preliminary results

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Background

Guidelines on maternal phenylketonuria recommend maternal phenylalanine concentrations at 120–360 $\mu\text{mol/L}$. Yet, few studies have examined prenatal phenylalanine levels in relation to early neurodevelopment. Prechtl introduced the General Movements Assessment (GMA), based on infant general movements (GMs), assessed in the first 5 months of life as a predictive tool for later neurocognitive development.

Objective

Our study investigated whether infant GMs could further optimize advice on maternal phenylalanine levels throughout pregnancy

Design/methods

Seven mothers with phenylketonuria with their infants were included. GMs were recorded via video at one to two weeks and 12 to 16 weeks post term using Prechtl's GMA. The video evaluated whether movements were normal, poor repertoire, or cramped-synchronized with the first, and normal, atypical or abnormal with the second video.

Results

Maternal phenylalanine levels during pregnancy generally were within the recommended range, although phenylalanine was lower and with less fluctuation in case 7 compared to other cases, except for conception date itself. Three infants showed poor repertoire at 1-2 weeks, and six infants scored atypical at the second video, while infant 7 was the only one with complete normal scores.

Conclusion

This study introduced a non-invasive method to assess development in early infancy in relation to maternal blood phenylalanine levels. Even though maternal phenylalanine levels were generally in range, only infant 7 scored normal at all evaluations, with less fluctuation, lower mean, median, max maternal phenylalanine levels. While larger studies are needed to validate predictive utility, GMs, as easily collected with videos in early infancy, may help to further optimize advice on maternal phenylketonuria.

Uncertainty Representation in Machine Learning and Humans in Grasping Task Using EEG

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Background

Representing uncertainty is significant for adaptive motor decisions in dynamic environments, especially when the costs of choosing wrong action is high. During decision-making, brain signals showed dynamics of accumulating noisy evidence until some bound. In human EEG, centro-parietal positivity (CPP) demonstrates similar characteristics while also being linked to decision confidence. On the other hand, machine learning (ML) research is also focusing increasingly on uncertainty quantification (UQ). In this respect, uncertainty is sometimes disentangled as aleatoric and epistemic. The first one is related to irreducible randomness inherent to data itself, while the latter refers to model incompetence in properly learning to execute the given task and can be reduced by more training. Additionally, some UQ methods disentangle uncertainty in vacuity and dissonance, which refer to lack of knowledge and presence of conflicting information respectively. However, it has yet to be examined if uncertainty in ML systems actually align with human judgements. Through brain-computer interfaces (BCIs) as a bridge between machine learning and EEG, one can investigate how well uncertainty in artificial and biological systems are comparable.

Objective

In this study, it is aimed to investigate the relationship of uncertainty in different levels, ranging from EEG, metacognitive evaluations, and ML classifiers in the BCI paradigm. With this study, we will provide additional insights about a second-order evaluation for the classifiers that is more aligned with human-type of uncertainty evaluation.

Design/methods

Participants will watch ambiguous grasping videos depicting three different types of grasp (pincer, precision, power). Using a staircase procedure powered by Quest+, the optimal difficulty level will be determined for each grasp type before the experiment. Subjects will decide during these displays for which grasp they should execute subsequently. After executing the chosen grasp, they will be asked to report how confident they felt (not confident at all, somehow confident, very confident) during grasping. CPP activity will be evaluated from a video observation interval. BCI classifiers that output the grasp type and its associated uncertainty will be trained from EEG signals during grasp execution.

Results

It is expected to see that CPP amplitude and rising slope will differentiate between correct and incorrect trials with respect to the following grasp. Additionally, we expect CPP peak amplitude to be larger for trials participants rated as highly confident during grasp execution. For the relationship with ML classifier uncertainty, CPP amplitude is expected to covary with vacuity, since lack of sufficient evidence may lead to higher vacuity and lower CPP activity. For metacognitive judgements on how participants felt during execution, we expect it to correlate with aleatoric uncertainty estimates, since the same underlying problem of noise (or variability) for that trial may lead to low confidence and high aleatoric uncertainty.

Conclusion

We believe that utilizing classifiers with high classification accuracy is a limited perspective and explainable ML algorithms are crucial to advance human machine collaboration. Therefore, evaluating uncertainty as a high-level variable that should align between human and classifier-level representation is helpful to develop adaptive, human-aware BCI systems.

Emotion Recognition and Suicide Risk in Psychiatric Disorders: A Multimodal MRI Study

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Background

Patients with psychiatric disorders have an increased risk of suicide, and exhibit deficits in recognizing and describing emotions and complex mental states in themselves and others. When individuals have difficulty identifying and regulating emotional experiences and mental states, negative emotions tend to be amplified, adaptive regulatory strategies are reduced, and sensitivity to interpersonal stressors and frustration is heightened, thereby increasing social isolation and social exclusion. These maladaptive cognitive patterns may weaken the psychological buffer that typically prevents suicidal ideation from escalating, thereby increasing suicide risk.

Objective

The present study aimed to investigate emotion recognition abilities in patients with psychiatric disorders with suicidal behavior, as well as the neural correlation and pathophysiological mechanisms linking functional and structural brain abnormalities to suicidality.

Methods

We recruited psychiatric patients with recent suicide attempts (SP = 29), psychiatric patients without a history of suicide attempts (PC = 24), and non-psychiatric controls (NC = 24), and conducted structural and functional MRI during the Reading the Mind in the Eyes Task (RMET). We compared gray matter structure and task-related activation during the RMET among the three groups. Subsequently, regression analyses were used to examine associations with affective measures.

Results

Gray matter volume of the middle temporal gyrus was significantly reduced in the PC group compared with the NC group, but no volumetric abnormalities were observed in the SP group. Regression analyses indicated that the gray matter volume of several regions, including the medial orbitofrontal cortex, postcentral gyrus, and middle temporal gyrus, was associated with alexithymia scores, emotional awareness, and suicidal thoughts. During the RMET, no significant group differences were observed in either behavioral performance or brain activation. However, task-related activation in the medial frontal gyrus was related to the Positive and Negative Syndrome Scale, hopelessness and suicidal thoughts, particularly in the SP group. Further mediation analysis showed that hopelessness significantly mediated the association between frontal activation and suicidality.

Conclusions

No structural and functional brain abnormalities were associated with previous suicidal attempts in people with psychiatric disorders. However, we underscore the critical role of the frontal lobe, particularly the medial prefrontal regions in the recognition and regulation of complex emotions and mental states, including hopelessness, in individual transitions to higher suicidal risk. These complex relations may inform interventions aimed at improving emotional cognition and regulation to lower hopelessness and thereby lowering suicidal risk in psychiatric populations.

The molecular signature of insomnia in major depressive disorder: A proteomic approach

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Background

Insomnia is a prevalent sleep disorder in major depressive disorder (MDD) that contributes to its etiology and unfavorable clinical course. Elucidating the molecular signature of insomnia in individuals with and without MDD could enhance understanding of this clinically relevant relationship.

Objective

We aimed to investigate whether insomnia is associated with serum proteomic analytes and whether these associations depend on MDD status.

Design/methods

Healthy controls, individuals with current MDD, and remitted MDD (N = 1447) from the Netherlands Study of Depression and Anxiety (NESDA) were assessed for insomnia using the Women's Health Initiative Insomnia Rating Scale. Serum levels of 172 analytes were measured (multi-analyte immunoassay). Associations between insomnia status and analyte levels were examined using linear regression. Interaction analyses tested whether associations differed across MDD diagnostic groups, with and without adjustment for relevant covariates.

Results

Insomnia was associated with 55 analytes ($p < .05$). Five remained significant after covariate adjustment (transthyretin, matrix metalloproteinase-10, phosphoserine aminotransferase, complement factor H-related protein 1, leptin), independent of MDD status. An interaction between insomnia and MDD status was observed for 13 analytes, and for 12 analytes after covariate adjustment. Several associations were exclusive to healthy controls, and fewer to current and remitted MDD.

Conclusion

Insomnia is associated with mechanisms previously implicated in MDD, including metabolic, immune, and neuroendocrine processes. For most analytes, there is no evidence of moderation by MDD status. Many associations are influenced by other factors and have a high false discovery rate. More research is needed to clarify the complex interplay of demographic, symptomatic and clinical characteristics influencing these molecular processes.

Generic care modules for the visual complaints of people with multiple sclerosis

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Background

Visual complaints are often experienced by people with multiple sclerosis (pwMS). These include blurry vision, reduced contrast, reduced depth perception, and some pwMS need more light while others are negatively affected by light. These complaints can influence many aspects of pwMS' daily life. There is a lack of generic rehabilitation for these visual complaints. Often many visual and neuropsychological assessments are done before pwMS meet with an occupational therapist at Royal Dutch Visio, but much of the advice given is the same.

Objective

Creating generic care modules to minimize the impact of visual complaints on the daily lives of pwMS and to decrease the burden of the rehabilitation on pwMS and the healthcare system.

Design/methods

To create the modules, a multidisciplinary team was assembled including occupational therapists, neuropsychologists, social workers, an optometrist, a clinical physicist, a digital accessibility expert and most importantly, pwMS. This large team was divided into four smaller teams, each working on one topic. The modules were created using a variety of design-centered thinking methods namely: brainwriting, six thinking hats, low-fidelity prototyping, and high-fidelity prototyping. The modules are delivered online via a telerehabilitation platform where interaction with healthcare providers is possible.

Results

Four generic care modules addressing psychoeducation, daily life, fatigue and energy balance, and lighting were developed. The modules support pwMS in independently managing visual complaints and integrating strategies, tips and adaptations to minimize the impact of these visual complaints on their daily lives. There are homework assignments in each module to ensure interaction with the care providers, to allow participants to practice implementing the advice into their daily life, and to increase adherence among participants.

Conclusion

By creating these modules, this project aims to fill the gap in existing neurovisual rehabilitation for visual complaints in pwMS. The use of a multidisciplinary team and design-centered methods offers patient-centered solutions that are expected to improve the quality of life for pwMS. Later phases of this project will include a feasibility study and a pilot study to determine the effectiveness of the modules.

BATMAN: Antibiotics Against Amyloid Angiopathy: A Randomized, Double-Blind, Placebo-Controlled Trial of Minocycline in Sporadic and Hereditary Cerebral Amyloid Angiopathy

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Background

Cerebral amyloid angiopathy (CAA) is a major cause of intracerebral hemorrhage and vascular dementia. CAA is characterized by amyloid- β 40 deposition in cerebral vessels, which may induce chronic neuroinflammation. Minocycline has anti-inflammatory properties.

Objective

This study investigated whether three months of treatment with minocycline reduces inflammatory cerebrospinal fluid (CSF) biomarkers and stabilizes radiological markers of CAA in sporadic CAA (sCAA) and hereditary Dutch-type CAA (D-CAA).

Design/methods

In a double-blind, placebo-controlled randomized trial, 60 participants (12 D-CAA, 48 sCAA) were assigned to minocycline or placebo. CSF biomarkers of neuroinflammation and gelatinase activity (IL-6, MCP-1, IBA-1, MMP-2/9, VEGF) were collected at baseline and after three months. 7T-MRI scans were also obtained, at baseline and after three months, and were assessed for white matter hyperintensities, enlarged perivascular spaces, cerebral microbleeds (CMBs), and cortical superficial siderosis (cSS).

Results

Complete MRI and CSF data at follow-up were available for 46 and 54 participants, respectively. CSF analyses demonstrated increased levels of IBA-1 and MMP-2 in the minocycline group ($P=0.007$, $\beta = 8.997$, 95% CI = [2.47 ; 15.52] and $p = 0.023$; $\beta = 1.11$; 95% CI [0.16 ; 2.06] respectively). Preliminary MRI analyses (without unblinding) indicated radiological progression, with CMB progression in 42 of 46 participants and cSS progression in 10 of 34 participants with cSS present at baseline. Analyses of within-group progression are ongoing.

Conclusion

Three months of minocycline treatment did not reduce CSF biomarkers of neuroinflammation; instead, MMP-2 and IBA-1 levels were higher in the minocycline group. Preliminary MRI findings indicate ongoing radiological progression independent of treatment allocation.

Cognitive profiles in young-onset dementia: a systematic review and meta-analysis

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Background: Young-onset dementia (YOD) can present with heterogeneous and atypical cognitive profiles, causing diagnostic delays. Establishing these cognitive profiles can improve recognition of YOD and support differential diagnostics.

Objective: This project aims to establish the cognitive profiles of thirteen types of YOD based on the scientific literature.

Design/methods: This systematic review and meta-analysis aimed to include all articles investigating YOD and cognition. Cognitive profiles of thirteen types of YOD from the spectra of Alzheimer's disease, frontotemporal dementia, Parkinson-plus, vascular disease, and Lewy Body dementia were established, compared to healthy control participants. Cognition was assessed using performance-based neuropsychological tests in ten cognitive domains, divided into their respective subprocesses. A meta-analysis was performed on articles with sufficient quantitative information.

Results: The search yielded 16258 articles. There was substantial agreement in title and abstract screening (observed agreement=0.94, κ =0.70). 890 articles (5.5%) were included for full-text screening, comprising 1688 patient groups. Representing more than half of all patient groups were behavioural variant frontotemporal dementia, Alzheimer's disease dementia, and semantic variant primary progressive aphasia. Following were nonfluent variant primary progressive aphasia, logopenic variant primary progressive aphasia, and progressive supranuclear palsy, making up a quarter of all patient groups. The least research has been performed on atypical Alzheimer's disease dementia, vascular dementia, Parkinson-plus dementia, and Lewy Body dementia. Additionally, certain cognitive domains were selectively assessed in particular patient groups. Social cognition was, for example, relatively frequently measured in behavioural variant frontotemporal dementia compared to other types of YOD.

Conclusion: We have established distinct cognitive profiles of common neurodegenerative types of YOD. These cognitive profiles can support earlier recognition of YOD and can inform the neuropsychological assessment in clinical settings, thereby reducing the time between symptom onset and diagnosis.

Characterization of astrocyte markers in white matter multiple sclerosis lesions

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Background

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating and neurodegenerative disease of the central nervous system. Focal white matter lesions (WMLs) are pathologically classified by the degree of demyelination and inflammation, as active, mixed active/inactive, inactive and remyelinated. Astrocytes, displaying heterogeneity within and across WMLs, play an important role in MS pathology. In active lesions and mixed active/inactive lesion rims, reactive fibrous astrocytes become hypertrophic likely supporting remyelination. Scar astrocytes dominate in mixed active/inactive lesion cores and inactive lesions, forming glial scars that impede remyelination.

Objective

By using snRNAseq we identified different astrocyte (sub)states in WMLs including grey matter-like astrocytes. Our recent spatial transcriptomic analysis showed differences in astrocyte marker gene expression with enrichment of distinct astrocyte (sub)states in either the core or the rim of lesions. Here, we aim to validate these findings at the protein level by examining grey and (reactive) white matter astrocyte markers in distinct WMLs and lesion-free white matter.

Design/methods

Post-mortem brain tissue from MS patients and non-neurological controls was analysed. Immunohistochemistry was performed on paraffin-embedded sections using antibodies against grey matter (GLT1, GLUL) and (reactive) white matter (CD44, GFAP, vimentin) astrocyte markers. Descriptive and quantitative analysis were applied to lesion rims, cores and surrounding perilesional white matter. Western blotting was conducted on fresh frozen samples to quantify astrocyte marker expression.

Results

Cells harboring GFAP and VIM were observed in all WMLs. CD44⁺-cells were present in active lesions and mixed active/inactive lesion rims, but not always detected in mixed active/inactive lesions cores and inactive lesions. GLT1⁺-cells were present in active and inactive lesions and more in mixed active/inactive lesion cores compared to lesion rims. GLUL⁺-cells were present in active and inactive lesions and more in mixed active/inactive lesion rims compared to lesion cores. GLT1⁺- and GLUL⁺-cells were absent in lesion-free white matter.

Conclusion

Our preliminary findings indicate astrocyte heterogeneity between and within WMLs and support our transcriptomic evidence of grey matter-like astrocytes in WMLs. Ongoing quantitative analysis will further refine our understanding of astrocyte heterogeneity in WMLs. These findings will aid in unravelling the role of astrocyte subtypes in the transition to either successful remyelination or persistent demyelination in MS lesions.

Butyrate modulates inflammatory responses in human iPSC-derived microglial cells

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Background

Glyphosate, a broad-spectrum herbicide, is extensively used and generally considered safe for humans since the shikimate pathway it inhibits does not exist in human cells. However, exposure to glyphosate has been reported as one of the environmental risk factors for the development of Parkinson's disease (PD), possibly through alterations of the gut microbiome, though the underlying mechanisms remain unclear. Glyphosate exposure leads to a misbalance in gut metabolite release, particularly of the short-chain fatty acids, with a decrease in butyrate levels. Our study aims to investigate how butyrate could counteract PD-related inflammation.

Objective

To investigate whether butyrate is able to prevent inflammatory processes in human induced pluripotent stem cell (iPSC)-derived microglia-like cells (iMGLs) challenged with inflammatory stimuli.

Design/methods

In this study, we generated human iMGLs. The iMGLs were challenged with lipopolysaccharide (LPS) and interferon- γ (IFN- γ) in the presence or absence of sodium butyrate. Live-cell imaging with IncuCyte S3 was used to assess morphology, cellular reactive oxygen species (ROS) levels, and phagocytic activity. Measurement of Extracellular acidification rate (ECAR) was performed using XFe extracellular flux analyzer. Lactate release was quantified by a lactate dehydrogenase (LDH)-based enzymatic assay. Fluorescence signals of inducible nitric oxide synthase (iNOS) were measured by microscopy.

Results

Application of sodium butyrate to human microglia led to an elongated morphology in a dose-dependent manner following 16-24 h exposure. Butyrate could prevent the metabolic reprogramming mediated by LPS and IFN- γ , and attenuate ROS production and iNOS expression in the microglia challenged with LPS and IFN- γ , suggesting that butyrate could play an important role in reducing microglial activation observed in PD pathology. Interestingly, the phagocytic activity of microglia was unaffected by butyrate treatment.

Conclusion

Butyrate regulates the inflammatory response in human microglia, indicating that gut microbial metabolites can influence brain microglial activity. This suggests a mechanistic link whereby alterations in gut microbiota and their metabolic products may act as modulators of neuroinflammation associated with PD. Understanding this gut-brain axis could reveal novel therapeutic targets for controlling neuroinflammatory processes that contribute to PD pathogenesis.

Larger pupils are linked to enhanced visual, but not auditory, detection

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Background

In visual detection tasks, larger pre-stimulus pupil size is associated with improved performance. This improvement is attributed to both optical and arousal-related effects. The optical effect refers to the improved sensitivity that follows from an enlarged pupil allowing more light to enter the eye. The arousal effect refers to the improved performance that follows from a more optimal level of arousal, which is also reflected in the size of the pupil. In a recent EEG experiment, we discovered that these effects may be partially distinct.

Objective

To dissociate these effects, we explored the impact of pupil size on detection performance across different sensory modalities (visual and auditory). We hypothesized that in the visual condition the relationship between pupil size and accuracy would be roughly linear, reflecting the combination of arousal and an optical effect. Conversely, in the auditory condition, this relationship was expected to follow an inverted-U shape, representing only the arousal effect.

Design/methods

We collected pupil size and EEG data while participants performed a task consisting of detecting faint visual and auditory stimuli. Stimulus parameters (opacity and volume) were adjusted using a staircase procedure to maintain a performance level of 75% accuracy in both modalities.

Results

We found a significant interaction between pupil size and task modality in determining accuracy. As expected, in the visual condition pupil size showed an approximately linear relationship with accuracy, such that larger pupils were associated with improved detection performance. Conversely, in the auditory condition the relationship more closely resembled an inverted-U shape, with larger pupils being associated with decreased performance relative to intermediate pupils.

Conclusion

We conclude that in the visual condition performance is determined by a combination of a pupil-related optical effect and fluctuations in arousal, while in the auditory condition performance is mainly determined by fluctuations in arousal.

Psychosis and social media; A multidisciplinary integrative review

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Background

Social media are platforms allowing people to create and share posts and to connect with other users. Individuals with a psychotic disorder often experience difficulties with social functioning. Social media could be a valuable digital environment for them to maintain contact in an accessible way. However, the personal nature of social media posts may make them difficult to interpret, and how algorithms steer content visibility is difficult to understand. Research into social media use identified both benefits and risks.

Objective

The goal of the integrative review is to map out what is known about how and why individuals with a psychotic disorder use social media, and which relationships between social media and mental health- and psychosocial outcomes are known in this population.

Design/methods

Five databases are systematically searched for articles related to social media and psychosis. After deleting duplicates, abstracts, and full-text screening, 43 articles have been included in the final review. Analysis is done using the “constant comparison” methodology.

Results

Individuals with a psychotic disorder use social media at comparable rates to various control groups. Facebook is the most studied platform and often identified as the most used and most popular platform. Unique linguistic and visual attributes in posts created and shared by individuals with a psychotic disorder were identified. Many individuals state they notice a change in their social media use when symptoms emerge. Social media is used for information, to stay in touch with family and friends, and to give and receive support. Research shows a negative correlation between social media use and negative symptoms and severity of symptoms, and positive correlation between social media use and social and general functioning. Younger and more highly educated people used social media more.

Conclusion

Research indicates that social media can be an important digital social environment to study in a population of individuals with a psychotic disorder. It could provide essential information potentially supporting processes of diagnostics, screening, and management. Specific behavior likely leads to specific outcomes, and the effect individuals experience from social media use is personal and dependent on individual characteristics. Future research should focus on online identity development, characteristics of giving and receiving support on different platforms, causal relationships, and additional outcomes of interest.

Parietal NAAG and Glx show distinct associations with cognitive and memory performance in mild cognitive impairment

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Background

Alterations in glutamatergic metabolites are increasingly recognized as early neurochemical markers of cognitive decline in mild cognitive impairment (MCI), yet the extent to which distinct metabolites relate to specific cognitive domains remains unclear. Using proton magnetic resonance spectroscopy (¹H-MRS) acquired from the posterior parietal cortex, the present study examined whether glutamate–glutamine (Glx) and N-acetylaspartylglutamate (NAAG) concentrations were differentially associated with associative memory and executive performance in individuals with MCI. All participants met strict spectral quality criteria (Cramér–Rao lower bound $\leq 20\%$), and analyses controlled for age and voxel tissue composition.

Design/methods

Participants underwent proton magnetic resonance spectroscopy (¹H-MRS) in the posterior parietal cortex, and only spectra meeting strict quality criteria (Cramér–Rao lower bound $\leq 20\%$) were included. Cognitive assessment focused on associative memory using the Face–Name Associative Memory Exam (FNAME) and executive functioning using verbal fluency and Stroop interference. Spearman correlations and linear regression models were used to evaluate metabolite–cognition associations, with age and voxel tissue composition included as covariates.

Results

Parietal Glx showed robust and consistent associations with multiple aspects of associative memory. Higher Glx concentrations were significantly related to better delayed recall ($r = 0.42$, $p_{\text{FDR}} = 0.002$), immediate recall ($r = 0.33$, $p_{\text{FDR}} = 0.018$), spontaneous recall ($r = 0.36$, $p_{\text{FDR}} = 0.012$), and face–name matching performance ($r = 0.31$, $p_{\text{FDR}} = 0.026$). In regression analyses, Glx significantly predicted delayed recall, immediate recall, and matching performance in both unadjusted and adjusted models, with adjusted models explaining 24–30% of the variance. The association with spontaneous recall did not remain significant after covariate adjustment.

In contrast, parietal NAAG showed only modest associations with executive performance. A small positive correlation with verbal fluency ($r = 0.31$, $p_{\text{FDR}} = 0.046$) did not remain significant in regression analyses, and NAAG was not associated with Stroop interference in either unadjusted or adjusted models.

Conclusion

These findings indicate a clear dissociation between parietal Glx and NAAG in MCI. Parietal Glx is strongly linked to associative memory, whereas parietal NAAG shows limited relevance for executive functioning. Glutamatergic metabolism in the parietal cortex may therefore serve as a sensitive neurochemical marker of early memory impairment.

Evaluating the Brief Observation of Social Communication Change (BOSCC) Scores Between Interaction Partners

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Background

Assessing changes in autism-related behaviours is challenging due to variability across settings, observers, and interaction partners. The Brief Observation of Social Communication Change (BOSCC) was developed to sensitively detect subtle short-term changes in social communication and repetitive behaviours. While the BOSCC can be administered by different adults, it is unclear whether parent- and professional-led sessions yield comparable scores, limiting its interpretability and use in naturalistic, home-based assessments.

Objective

This study examined whether the BOSCC yields consistent scores when administered by parents versus professionals within the same home environment.

Design/methods

Forty-one toddlers (73% male; mean age 28.2 months) at elevated likelihood for autism spectrum disorder completed two BOSCC sessions at home: one parent-led and one professional-led, following identical procedures. The domains, Social Communication (SC), Restricted and Repetitive Behaviours (RRB), and Other Abnormal Behaviours (OAB), were scored by independent coders. Scores were compared using paired t-tests or Wilcoxon signed-rank tests, and consistency was assessed with correlations.

Results

No significant differences were observed between parent- and professional-led sessions for Total BOSCC scores or the SC, RRB, or OAB domains (all $p > .19$; Cohen's $d < 0.15$). Correlations were strong for Total ($\rho = 0.90$), SC ($\rho = 0.83$), and RRB ($r = 0.78$) scores, indicating high consistency. OAB scores exhibited only moderate correlation ($\rho = 0.33$), which became non-significant following outlier exclusion.

Conclusion

BOSCC reliably captures core autism-related behaviours (SC and RRB) irrespective of whether the session is led by a parent or a professional. Parent-led administration in the home is a valid and scalable approach for naturalistic behavioural monitoring and intervention assessment.

The Role of Sex and Ovarian Hormones in Sleep Loss-Induced Hippocampal Deficits

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Background: Sleep loss adversely affects hippocampal memory, primarily via effects on synaptic plasticity. Sex differences in sleep patterns and memory performance are observed across species, with emerging evidence that these are driven by the hormonal milieu of females. Indeed, higher estradiol levels in females are neuroprotective and contribute to enhanced hippocampal-dependent memory and synaptogenesis. In addition, estradiol suppresses sleep in nocturnal rodents. However, whether higher estradiol levels protect females against sleep loss-induced memory and synaptic deficits remains unknown.

Objectives: 1) To determine whether sleep loss-induced hippocampal deficits observed in males are also present in females, and whether sleep loss similarly impairs spatial working memory in both sexes; 2) To assess whether the estrous cycle modulates the effects of sleep loss in females.

Design/methods: C57BL/6J young adult male (n=22) and female mice (n=52) were assessed on working and long-term memory following six hours of sleep deprivation (SD). Mice were randomly assigned by sex to the experimental or control condition, with females tested either during proestrus (high estradiol levels) or estrus (low estradiol levels). Each animal underwent two test sessions to separately assess SD effects on novel arm recognition (NAR) and long-term object location memory (OLM). A third SD session was performed to assess differences in synaptic density in the CA1, which was quantified using Golgi-Cox staining. Blood samples were also collected to measure sex steroids and corticosterone responses to SD.

Results: Working memory in the NAR task was unaffected by SD in all groups, suggesting that a brief 6h SD does not impair spatial working memory. In contrast, OLM revealed a significant interaction between sex and SD condition. As previously reported, control males showed a stronger preference for the displaced object compared to SD males. In females, however, the effect depended on hormonal state: SD females in proestrus exhibited better long-term memory than control proestrus females, whereas SD had no detectable effect in estrus. In addition, preliminary Golgi-Cox analyses show that SD males and SD estrus females showed a reduction in CA1 mushroom spine density, while, proestrus females exhibited increased CA1 mushroom spine density after SD relative to proestrus controls. Finally, SD selectively elevated circulating corticosterone in females, independent of estrous phase, indicating a stronger physiological stress response to sleep loss in females. No differences in sex steroid levels were found between SD and control animals.

Conclusion: Males and females respond differently to acute sleep loss at both cognitive and synaptic levels. Importantly, the estrous cycle modulates these effects in females, with higher levels of estradiol in proestrus being protective against SD-induced impairments in hippocampal memory and structural plasticity. These results underscore the need to incorporate sex and hormonal state when studying the neurobiological consequences of sleep loss.

Voice and Speech Perception in Adult Hearing-Aid Users

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Background

The human voice carries critical information about a speaker's identity (e.g., gender, age, size) and emotional state, important aspects in daily communication. In listeners with normal hearing (NH), voice perception and vocal emotion recognition are shown to develop early in life, refine during adolescence, and mature in adulthood. However, for people with hearing loss, especially those who use hearing aids (HAs), the development of voice perception has been relatively understudied. While HAs amplify surrounding sounds and improve audibility, they must also compensate for the ear's mechanisms, affected by hearing loss. As a result, they can distort or compress the original acoustic information, thereby modulating the voice cues. Previous research has shown delayed and incomplete development of voice cues perception in children with HAs. However, it is not yet known how these skills evolve in adulthood, whether they continue to develop but in a delayed manner, plateau, or perhaps even decline over time. Further, voice cue perception could be affected by individual differences in age, hearing loss severity, duration of HA use, and cognitive and verbal skills.

Objective

This project investigates how adults with HAs perceive and integrate voice cues and vocal emotions, compared to adults without HAs. The study also aims to identify individual-level predictors of voice perception variability, with a focus on cognitive and verbal skills.

Design/methods

The study will include two age-matched adult groups: non-users of HAs (control group) and HAs users (target group). Participants will complete experimental tasks assessing voice cue discrimination, voice gender categorisation, vocal emotion recognition, and speech perception in noise. HA users will perform the experimental tasks twice, both with and without their HAs. Additional quantitative data will be collected to account for variability and potential confounding effects, and will include hearing screening, questionnaires on HA use and demographic information, and cognitive and verbal skills tests.

Results

We expect that adults using HAs will show reduced sensitivity to voice cues and lower accuracy in vocal emotion recognition compared to an age-matched control group. We expect the performance of the target group to improve when wearing HAs, but it will still not fully reach the levels of the control group. We also expect to find individual variability among HA users, with performance being predicted by age, HA experience, and cognitive abilities.

Conclusion

This study is expected to improve understanding of how hearing loss and HA use affect voice and speech perception in adulthood. Addressing this knowledge gap has implications for theoretical models of auditory processing and can also impact clinical practice through improvements in counselling, rehabilitation, and the development of HA technology.

Cumulative Stress and Cognitive Ageing: Human Evidence from China and the UK and a Translational Framework

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Background

Cognitive ageing is shaped not only by biological factors but also by life-course experiences. Psychosocial stress is a key yet understudied driver of cognitive decline, as most studies focus on single stressors or isolated life periods. In reality, stressors often accumulate across childhood and adulthood, potentially exerting stronger, domain-specific, and sex-dependent effects on cognition.

Objective

To investigate the associations between life-course and cumulative stress exposure and trajectories of global and domain-specific cognitive function, and to establish a translational framework linking human epidemiological findings to experimental mouse models.

Design/methods

We combined longitudinal data from two large population-based ageing cohorts: the China Health and Retirement Longitudinal Study (CHARLS, n = 5,922) and the English Longitudinal Study of Ageing (ELSA, n = 10,893). Life-course stress exposures during childhood, adulthood, and cumulatively were related to global cognition, memory, executive function, and orientation using mixed-effects models. Stratified analyses were conducted by sex and educational attainment. In parallel, ongoing mouse studies aim to elucidate the neurobiological mechanisms underlying stress-related cognitive vulnerability.

Results

Childhood stress was mainly associated with poorer memory performance, whereas adulthood stress predominantly affected executive function. Life-course stress exposure was related to declines across all cognitive domains. Under life-course stress, females showed greater vulnerability than males. Cumulative stress was consistently associated with executive dysfunction and, in longitudinal analyses, also with memory and orientation decline. In contrast to life-course stress, males appeared more vulnerable under multiple stress exposures. Higher educational attainment buffered the effects of single stress exposure but provided only limited protection against cumulative stress.

Conclusion

Accumulated stress across the life course is associated with accelerated and domain-specific cognitive ageing, with distinct sex- and education-related vulnerability patterns. These findings highlight the importance of stress reduction, early intervention, and sex-sensitive prevention strategies, and provide a translational framework for mechanistic studies in animal models.

Modelling glioblastoma-extracellular matrix interactions in vivo using zebrafish and atomic force microscopy

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Background

Glioblastoma (GB) remains the most aggressive adult brain tumor, characterized by rapid invasion and poor prognosis. While research has traditionally focused on genetic drivers of GB, there is growing recognition that extracellular matrix (ECM) alterations play a central role in tumor progression. GB is known to remodel its microenvironment, increasing tissue stiffness to as much as 35 kPa, conditions that have been shown in vitro to promote tumor cell migration and invasion. However, in vivo models that allow mechanistic investigation of ECM–GB interactions remain technically challenging.

Objective

Here, we aim to establish a zebrafish larval model for studying glioblastoma invasion in vivo and to characterize brain tissue stiffness as a baseline for investigating ECM-tumor mechanical interactions.

Design/methods

To address this, we established an orthotopic xenograft model in zebrafish larvae to study GB behavior within a live, developing brain. Human GB cells (U87, GG16, and GSC23) were transplanted into the midbrain of 3-day-old larvae, and their migration and invasion were monitored in real-time using confocal and light-sheet microscopy. Whilst tumor implantation had proved difficult, we in parallel used atomic force microscopy (AFM) to characterize the mechanical properties of healthy larval brains.

Results

Average midbrain stiffness does not significantly differ between timepoint of our experimental timespan (5-15-day-old larvae). Highest average stiffness was measured at 5 days (5.18 kPa), lowest average stiffness was measured at 13 days (2.86 kPa), indicating that zebrafish larval brain stiffness is comparable to healthy adult brain stiffness (1-2 kPa). No significant differences were observed across midbrain regions or hemispheres, indicating spatial consistency in brain stiffness during this timeframe.

Conclusion

Ongoing work focuses on xenografting GB cells to measure tumor-induced stiffness changes, as well as genetically modulating ECM components (fibronectin, collagen, and hyaluronic acid regulators) in GB cells to assess their impact on tissue mechanics and invasion dynamics.

Tracking Cognitive Functioning in Psychosis through Automated Speech analysis

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Background

Cognitive impairments are core features of psychotic disorders, yet the relationship between speech abnormalities and cognitive performance remains underexplored. Understanding these associations could inform neurobiological mechanisms and potentially provide surrogate markers for time-consuming cognitive testing.

Objective

To investigate whether automated speech features predict cognitive performance in psychosis, controlling for demographics and individual variability.

Design/methods

We analyzed 565 speech recordings from 362 patients with psychosis who completed the Brief Assessment of Cognition in Schizophrenia. Automated analysis extracted 132 speech features across acoustic, syntactic, and semantic domains, reduced to six dimensions via principal component analysis. Linear mixed-effects models examined speech-cognition associations, controlling for age, education, and gender, with random intercepts for participants. Model comparison used AIC and 5-fold cross-validation.

Results

Full models (demographics + speech) showed superior fit versus baseline across all cognitive domains (Δ AIC: 10.1-31.6). Speech features explained an additional 1.0-4.7% of variance beyond demographics. However, cross-validation revealed minimal out-of-sample prediction improvement (MAE change: -0.7% to +3.4%). Between-participant differences accounted for most explainable variance (R^2 conditional: 48-71%), with fixed effects explaining only 6-14%. Six speech-cognition associations survived FDR correction, including negative associations between verbal memory and verbal output/prosody features, and positive associations between processing speed measures and sentence length/semantic features. All speech effects were smaller than demographic predictors, with education emerging as the strongest predictor across domains.

Conclusion

Automated speech features show modest associations with cognitive performance in psychosis but provide minimal enhancement to prediction accuracy. The dominance of between-participant variance suggests stable individual differences primarily drive cognitive variability. Future research should explore theory-driven feature selection and potential moderating effects of medication and symptom severity.

Evaluating the efficacy of Theory of Mind training and language-based training in improving social cognition in children who wear hearing devices

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Background: Some children who are deaf or hard of hearing (DHH) and born to hearing parents experience delays in their development of Theory of Mind (ToM): the ability to attribute mental states (e.g., beliefs, desires, or emotions) to self and others (Schick et al., 2007). ToM comprises multiple subcomponents that are acquired throughout childhood, with more basic abilities (e.g., recognizing differing desires) being acquired at an early age and more complex abilities (e.g., understanding sarcasm) at a later age (Peterson et al., 2012). Lower ToM abilities in children who are DHH are correlated with decreased perceived popularity and increased perceived social isolation at school (Peterson et al., 2016). Factors that influence ToM performance include linguistic abilities (Bigelow et al., 2021) and executive functions (Austin et al., 2014). Children who wear a hearing device (i.e., a cochlear implant and/or hearing aids) were shown to perform similarly to children with normal hearing when tested on basic ToM subcomponents, but exhibited difficulties with more complex subcomponents (Choi & Jeong, 2023). Training ToM skills in children has been shown to be effective (Hofmann et al., 2016), but has not yet been examined in Dutch-speaking children with hearing devices.

Objective: The current project will evaluate the efficacy of two interventions in improving ToM abilities in Dutch-speaking children with hearing devices: (1) a ToM-focused group intervention, and (2) a language-focused individual intervention. We will examine ToM abilities in relation to vocal emotion recognition, linguistic abilities, executive functions, and speech perception.

Design/methods: We aim to recruit 64 Dutch-speaking children aged 5 to 12 years old with bilateral hearing loss (PTA >35 dB) who use a hearing device to participate in the study. Their ToM abilities and vocal emotion recognition will be assessed at three time points: four months prior to the intervention (pre-test one), shortly before the intervention (pre-test two), and shortly after the intervention (post-test). Additionally, their executive functions (specifically inhibition, switching, and planning), implicit language comprehension, and pragmatic profile will be measured to investigate their effects on ToM performance. Finally, semi-structured interviews will be held with parents of the participants to evaluate their experience with both interventions.

Expected results: We expect to observe a steeper increase in ToM performance after the intervention (pre-test two to post-test) compared to the period before the intervention (pre-test one to pre-test two). Furthermore, we expect better language abilities, executive functions, and speech perception to enhance potential individual gains in ToM abilities.

Conclusion: By evaluating the efficacy of a ToM-focused and language-focused intervention using both quantitative and qualitative measures, this project aims to contribute to improving the social well-being of children who are DHH and to support parents in making evidence-based decisions regarding their children's treatment and guidance.

Reliability-Weighted Bayesian Updating Explains Sequential Biases in Time Perception**Taku Otsuka**¹, Joost de Jong¹, Wouter Kruijne¹, & Hedderik van Rijn¹¹ Department of Experimental Psychology**Background**

Human perception is shaped not only by current sensory input but also by recent experiences. Sequential effects where the current percept is attracted toward the immediately preceding one provide a clear example. Such effects have been widely documented across domains, yet their computational basis remains elusive.

Objective

The present study employed a time perception task to test a central prediction of the Bayesian account, which proposes that sequential effects reflect an adaptive integration of past and present information weighted by their relative reliability.

Design/methods

We manipulated stimulus reliability by varying the signal-to-noise ratio of visual stimuli in a duration reproduction task, where participants reproduced the duration of a visual stimulus embedded in dynamic visual noise.

Results

We found that sequential effects were modulated by the reliability of the current and previous stimuli, consistent with Bayesian predictions. Moreover, this reliability-dependent effect was captured by a simple Bayesian model that sequentially updates the priors while incorporating the sensory noise of the inputs (i.e., a Kalman filter).

Conclusion

These findings provide direct empirical evidence for reliability-based integration in human duration judgements.

Morphological fluency networks: A methodological study

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Background

Language tasks can be used to create word networks. In a verbal fluency task, participants have one minute to name as many words as possible (e.g., animals). Generally, people produce similar words together in so-called clusters (e.g., pets, farm animals). Words that are named by multiple participants become nodes in the network, with connections (i.e., edges) between words that are produced within a particular distance from one another (i.e., window size).

Objective

For a newly constructed morphological fluency task, we aimed to investigate whether networks of words in response to nouns and verbs and to cue words with a large or a small morphological family size had distinct structures. Furthermore, the methodological aim was to understand how to compare groups of different-sized networks.

Design/methods

One hundred participants (19-35 years old) produced as many morphologically related words as possible for 24 Dutch words in 60 seconds per cue (e.g., for *instrument*: *instruments*, *instrumental*). For each cue, the mean and standard deviation of the size of morphology-based clusters were used to determine the window size for the corresponding network (ranging 2-6). The following metrics were extracted from the 24 networks: numbers of nodes (N) and edges (E), clustering coefficient (CC), and modularity (Q).

Results

Networks for cue words with a large compared to a small morphological family size contained significantly more nodes ($F(1,20) = 21.63, p < .001$). In terms of CC and Q, the majority of the networks were structured differently from random networks with the same N and E. Bootstrapping analyses with equal-sized partial networks revealed an interaction effect of word class and family size on Q, with largest Q for verb cues with a small morphological family size ($SE = 0.107, z = 1.985, p = .047$).

Conclusion

Networks constructed with the morphological fluency task generally include meaningful connections between words, showing some structural differences between cue conditions. Nevertheless, networks were constructed with varying window sizes, and some networks may have been too small for the partial network analyses. These limitations could affect between-network comparisons and should be addressed in future analyses.

EVT in patients with tandem lesions: effect of CAS and EVT devices
a cohort study from the EVA-TRISP collaboration

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Background

15–20% of patients with acute ischemic stroke (AIS) due to anterior large vessel occlusion present with ipsilateral extracranial carotid artery stenosis >50% or occlusion, termed tandem lesions (TLs). The optimal endovascular treatment (EVT) strategy for TLs remains uncertain, particularly regarding carotid artery stenting (CAS) and thrombectomy techniques.

Objective

This study compared outcomes in TL patients treated with or without CAS during EVT and the impact of different thrombectomy approaches (aspiration alone [AA], stent retriever alone [SRA], or combined approach [CA]).

Design/methods

EVA-TRISP is a large international multicenter cohort study including consecutive AIS patients treated with EVT, 2016–2023. Outcomes included 3-month modified Rankin Scale (mRS), good functional outcome (mRS 0–2), complete angiographic recanalization, symptomatic intracranial hemorrhage (sICH), and all-cause mortality.

Results

Among 13,702 EVT-treated patients, 1,545 (11.3%) had TLs; 596/1,545 (39%) underwent CAS. CAS was associated with higher odds of better functional outcome (adjusted odds ratio [aOR] 1.33, 95% CI 1.09–1.62) without increased sICH or mortality. AA was used in 28.1%, SRA in 26.8%, and CA in 45.1%. SRA and CA were associated with higher odds of complete recanalization (aOR 1.96 [95% CI 1.38–2.78] & 1.99 [95% CI 1.48–2.67]), compared to AA. CA was not associated with functional benefit but rather with sICH (aOR 2.50, 95% CI 1.28–4.89).

Conclusion

CAS during EVT was associated with improved functional outcomes in TL patients without increased hemorrhagic risk or mortality. Stent retriever use improved recanalization, while combined techniques increased sICH risk without added clinical benefit.

Alpha-synuclein induces oxidative stress in dopaminergic neurons via NOX4 activation**Maria João Caiado^{1,2}, Amalia Dolga², Wilfred den Dunnen¹**¹ Department of Pathology and Medical Biology, UMCG² Department of Molecular Pharmacology, University of Groningen**Background**

Parkinson's disease (PD) is characterised by alpha-synuclein inclusions in dopaminergic neurons of the substantia nigra. These neurons experience high levels of oxidative stress often stemming from mitochondrial dysfunction, leading to neurodegeneration. Notably, NOX4, primarily located in mitochondria, mediates the production of reactive oxygen species (ROS). However, how alpha-synuclein inclusions impact these pathways remains unknown.

Objective

We aim to investigate how alpha-synuclein may be affecting ROS production in dopaminergic neurons and how targeting oxidative stress pathways may confer neuroprotection in PD.

Design/methods

To investigate this, a tissue microarray (TMA) was constructed from 10 PD patients and 6 age-matched controls (aged 58-88). Then, the TMA slide was immunolabelled with NOX4 and pixel density scoring was used to measure its expression in neurons with and without alpha-synuclein from PD cases, compared to controls. A separate TMA slide was immunolabelled with Tyrosine Hydroxylase, followed by whole transcriptome sequencing of dopaminergic neurons. In vitro, LUHMES (dopaminergic neurons) were challenged with alpha-synuclein fibrils, and then ROS production was measured. Next, NOX4 was pharmacologically inhibited under those conditions to assess its potential against alpha-synuclein-induced oxidative damage.

Results

Positive pixel-density scoring revealed higher NOX4 expression in PD neurons compared to controls. Transcriptomic analyses showed higher ROS production and mitochondrial dysfunction in dopaminergic neurons from PD cases, compared to controls. In LUHMES, alpha-synuclein increased ROS production, but inhibiting NOX4 rescued these effects.

Conclusion

These results demonstrate that alpha-synuclein renders dopaminergic neurons more susceptible to oxidative damage and mitochondrial dysfunction, whereas targeting NOX4 confers neuroprotection. Thus, our findings highlight mitochondria as central in PD pathophysiology and NOX4 as a key target in promoting neuronal resilience.

A flow-cytometric reporter system to predict protein homeostasis collapse in CAG-expansion diseases

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Background

Huntington's Disease (HD) is caused by expanded CAG repeats in the huntingtin (HTT) gene, resulting in the production of aggregation-prone polyglutamine (polyQ) proteins that lead to neurodegeneration. The disease onset can be predicted by the CAG-repeat length. However, substantial inter-individual variability in age of onset suggests that CAG-repeat length alone is insufficient to predict age of onset. Additionally, HTT-PolyQ aggregation is correlated with CAG-repeat length, but aggregation takes place too late to be useful as a predictive marker for disease. Loss of protein homeostasis, a hallmark of aging and neurodegenerative diseases, is thought to precede HTT-polyQ aggregation and thereby possibly also disease onset. Therefore, we hypothesize that inter-individual differences in protein homeostasis explain the variability in age of onset and can be used as a predictive marker.

Objective

We aim to measure the protein homeostasis status prior to HTT-polyQ aggregation using various reporters for protein homeostasis in an HD cell model with variable CAG-repeat lengths.

Design/methods

We developed a flow cytometric assay that allows us to correlate HTT-polyQ expression with protein homeostasis reporter levels. By combining this assay with Pulse-Shape Analysis (PulSA), we can identify and differentiate cells with HTT-polyQ aggregates from cells that have not yet formed aggregates.

Results

We observed increased protein homeostasis stress upon expression of HTT-polyQ, which positively correlates with HTT-polyQ expression levels and CAG-repeat length. Strikingly, protein homeostasis stress was detectable prior to HTT-polyQ aggregation. This reporter assay allows us to test whether inhibitors of HTT-polyQ aggregation, which were previously evaluated only for their anti-aggregation activity, also reduce protein homeostasis stress. Preliminary data show that DNAJB6, a molecular chaperone with anti-aggregation activity for HTT-polyQ, decreases HTT-polyQ-induced protein homeostasis stress in cells before aggregation.

Conclusion

This novel reporter assay allows for simultaneous measurements of HTT-polyQ expression levels, aggregation state, and protein homeostasis status. Our data show that HTT-PolyQ causes protein homeostasis stress even before aggregation. Furthermore, DNAJB6 is not only able to reduce the aggregation of HTT-polyQ but also reduces toxicity of soluble HTT-polyQ. We will exploit this reporter system to evaluate the effect of genetic and chemical inhibitors of HTT-polyQ aggregation on protein homeostasis status, and to extend comparative studies to other CAG-expansion diseases (CureQ consortium).

Epidural Local Anaesthetic Bolus After Lumbar Fusion: Added value for Postoperative Pain Relief?

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Background: Postoperative pain remains a serious concern after posterior lumbar interbody fusion (PLIF). Intraoperative epidural boluses of local anesthetics (LA) have been proposed to reduce pain while limiting opioid-related adverse effects. However, available evidence remains inconsistent.

Objective: This study evaluated the added value of this bolus in reducing postoperative pain at the post-anaesthesia care unit (PACU) after PLIF.

Design/methods: A retrospective study of 147 patients undergoing PLIF was conducted. The control group received standard opioid-based analgesia, while the bolus group received opioid-based analgesia with an additional epidural LA bolus at the end of surgery. The *primary outcome* was static (in rest) and dynamic (in movement) pain intensity (Numeric Rating Scale, NRS) at the PACU, analysed with two-sided Mann-Whitney tests. *Secondary outcomes* were ward NRS, opioid consumption (Morphine Milligram Equivalents, MME), PACU and hospital length of stay (LOS), and analgesia- and surgery-related complications within 1 month. Additional analyses included univariate and multivariable regression models adjusting for age, sex, BMI, ASA classification, preoperative opioid use, previous spinal surgery, screw trajectory, and cardiac comorbidities.

Results: A total of 67 control patients and 80 bolus patients were analyzed. The groups were similar in age and sex but differed in BMI, ASA classification, prior spinal surgery, and screw trajectory. *Primary outcome:* No significant differences were observed in static ($U=2439.0$, $p=0.60$) or dynamic ($U=1944.5$, $p=0.48$) PACU NRS. After adjustment, static (multivariable, $\beta=-0.36$, $p=0.54$) and dynamic NRS (multivariable, $\beta=-0.57$, $p=0.34$) remained similar. *Secondary outcomes:* Ward NRS and opioid consumption at the PACU did not differ; however, MME/hour on postoperative day 1 was lower in the bolus group (multivariable, $\beta=-0.26$, $p=0.02$). PACU LOS, hospital LOS, and analgesia-related complications were similar. Surgery-related complications <1 month were not increased.

Conclusion: This study showed no added value of administering an epidural LA bolus after PLIF for pain management at the PACU, as pain and opioid consumption were comparable between the groups.

Speech-Music Therapy in the treatment of childhood apraxia of speech: a multiple single-subject treatment study

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Background: Speech-Music Therapy for Aphasia (SMTA), a combination of speech and music therapy, is used in the treatment of children with childhood apraxia of speech (CAS). Children with CAS experience problems in functional communication and social participation because their intelligibility is negatively impacted by inappropriate prosody, segmental errors and disrupted co-articulation.

CAS often co-occurs with neurodevelopmental disorders, such as intellectual disability, leading to additional challenges in daily communication. However, most treatment studies so far exclude children with CAS and neurodevelopmental disorders.

SMTA is applied in the treatment of children with CAS with and without intellectual disability. The theoretical foundations for the use of music in the treatment of CAS include overlap in neurological processing of speech and music as well as overall effects of music on mood, motivation and attention.

Objective: The aim of this study is to evaluate SMTA in the treatment of CAS in children with and without co-occurring neurodevelopmental disorders.

Design/methods: A multiple single-subject study was conducted, including four children with CAS and intellectual disability and two children with CAS without intellectual disability. The protocol included pretest, baseline, treatment, posttest, and follow-up after two months of no speech planning and programming treatment. SMTA was conducted twice a week in 30-minute sessions for ten weeks. Treatment items were selected to be relevant for functional communication and appropriate for individual speech goals. For each item, a unique melody was composed that was used in a fixed protocol starting with singing, followed by rhythmical chanting and speaking. Outcome measures included segmental accuracy in picture naming, non-word imitation, an individual probe task, diadochokinesis and spontaneous speech; consistency in word and non-word repetition; and intelligibility, communicative participation and communicative attitude.

Results: Results indicated that improvement differed across children. The children with CAS and intellectual disability showed improvement in segmental accuracy in their individual probe task of trained items. There was little to no generalization to segmental accuracy in picture naming. There was improvement in intelligibility and functional communication.

The children with CAS without intellectual disability improved on their individual probe task and showed generalization to unrelated speech tasks such as picture naming. They also showed improved consistency in word and non-word repetition and diadochokinesis and improvements in intelligibility and communication participation.

Conclusion: SMTA is applied in the treatment of children with CAS with and without intellectual disability. Results of a multiple single-subject design showed different results for children with and without intellectual disability. All children improved on an individual probe task of the trained items, but generalization to unrelated speech tasks only occurred in children with CAS without intellectual disability. However, all children improved on measures of intelligibility and communicative participation, suggesting that training functional relevant items with SMTA can impact communicative participation in children with CAS, with and without intellectual disability.

Trajectories of Clozapine Concentrations in Women Across Menopausal Age

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Background

During menopause, estrogen levels change dramatically, which may decrease clozapine blood concentrations in women via estrogen's inhibitory effect on CYP1A2 activity. This reduction could contribute to increased relapse rates seen in older women with psychotic disorders.

Objective

Identify sex-specific longitudinal trajectories of clozapine blood concentrations in men and women aged 40-60 using latent class growth analysis.

Design/methods

Clozapine blood concentration data were retrieved from the University Medical Center Groningen, the Netherlands. A total of 982 patients (720 men, 262 women), aged 40-60, with 17 104 measurements, were included for analyses. Latent class growth analysis (LCGA) assessed clozapine trajectories by sex, while linear mixed-effects models (LMEM) assessed sex differences between trajectory classes.

Results

The optimal LCGA model (7-quantile splines) identified 3 clusters. Most women (n = 157, 60%) showed a decline in clozapine levels from 520 to 400 µg/L between the ages of 40-60. In contrast, most men (n = 392, 54%) had stable levels (mean 460 µg/L). Two other trajectories appeared in both sexes: a mild increase starting at age 45 (men: n = 272, 38%; women: n = 97, 37%) and a marked increase from 40 to 60 (men: n = 56, ~8%; women: n = 8, ~3%). LMEM showed significantly higher levels in women than men with stable trajectories (estimate = 177.03, t = 2.62, P < .01). A significant age-by-sex interaction (estimate = -0.067, t = -2.63, P < .01) suggested these differences varied over time.

Conclusion

Sex-specific longitudinal trajectories of clozapine concentrations showed declines in 60% of women aged 40-60, while most men remained stable. As decreasing blood levels could increase relapse vulnerability, monitoring clinical efficacy and side effects is warranted during menopause.

Improving Cognition in Severe Mental Illness by Combining Cognitive Remediation and Transcranial Direct Current Stimulation: Study Protocol for a Pragmatic Randomised Sham-Controlled Multi-Centre Trial (HEADDSET+)

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Background

Individuals with severe mental illness (SMI) frequently experience challenges in daily life, often attributable to cognitive impairments. Cognitive rehabilitation interventions can be implemented to enhance thinking abilities and improve functional outcomes. Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that may promote neural plasticity and, therefore, may enhance learning.

Objective

This trial aims to determine whether individuals with SMI who need supported housing can improve cognitive and daily functioning after following cognitive remediation (CR). Next, this trial evaluates whether CR combined with tDCS will enhance the effect of CR alone. Lastly, this trial will investigate the subjective experience of the CR intervention. We expect that participants will improve in goal attainment and cognitive and daily functioning.

Design/methods

In this pragmatic, triple-blinded, randomised, sham-controlled multi-centre trial, we will compare the experimental group (CR + active tDCS) with the control group (CR + sham tDCS). 126 participants with SMI will receive 16-20 weeks of twice-weekly CR (32-40 sessions of 30-45 minutes) combined with active (N = 63) or sham tDCS (N = 63), separated over five cohorts. We will recruit participants aged between 18 and 65 with SMI residing in supported living facilities. Functional, cognitive, and clinical outcome assessments will be performed at baseline, post-16-week waiting period, post-treatment, and 6-month post-treatment. Additionally, post-treatment participants will be asked to engage in an in-depth interview to evaluate their meta-cognitive skills and subjective experience of the treatment.

Results

Preliminary results from the post-treatment effects, along with insights from in-depth interviews conducted in the first cohort (N = 15) as well as post-16-week waiting period effects for goal attainment (including the second cohort, N ≈ 40) will be presented.

Conclusion

This randomised controlled trial will investigate the efficacy of CR and tDCS in enhancing recovery in people with SMI. If the intervention proves to be effective, it has the potential to be implemented into standard care for service users requiring long-term support.

Trial registration: ClinicalTrials.gov (NCT06378463). Prospectively registered on April 17, 2024.

Predicting inattention and hyperactivity-impulsivity symptom trajectories of ADHD using random forest classification in the Adolescent Brain Cognitive Development Study

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Background

Despite well-established genetic and environmental risk factors for attention deficit–hyperactivity disorder (ADHD), it remains unclear why children show different developmental trajectories of ADHD symptoms.

Objective

This study aimed to investigate distinct developmental trajectories of inattention and hyperactivity-impulsivity symptoms and to identify predictors of these trajectories at the transition from childhood to adolescence.

Design/methods

Data were drawn from the longitudinal Adolescent Brain and Cognitive Development dataset ($n = 11875$) and included yearly measures from baseline to wave 3 (ages 9-10 to 12-13). Growth mixture models were applied to the inattention and hyperactivity-impulsivity symptoms of the ADHD subscale of the Child Behavior Checklist to identify trajectories. Random forest classification models were then trained to predict these trajectories using genetic, familial, demographic and behavioral variables previously linked to ADHD. Logistic regression analyses were conducted to determine the direction of associations.

Results

Three trajectories were identified for inattention (non-affected, moderate, and persistent-high), and five for hyperactivity-impulsivity (non-affected, low, worsening, improving, and persistent-high). Key predictors for both domains included male sex and higher externalizing symptoms, family conflict, and polygenic risk scores of ADHD, distinguishing affected from non-affected children. Additional distinguishing factors were lower secondary caregiver acceptance (inattention) and family income (hyperactivity-impulsivity). Further, a persistent-high inattention trajectory was associated with negative school experiences and more internalizing symptoms, while worsening and persistent-high hyperactivity-impulsivity trajectories were linked to slower pubertal development.

Conclusion

This study supports the distinction between inattention and hyperactivity-impulsivity trajectories, which may be shaped by domain-specific factors. Nevertheless, at its core, both ADHD domains appear to be associated with shared factors, including biological and environmental, in the distinction between non-affected youth and those with ADHD symptomatology.

Effects of cumulative early life stress and social stress during adulthood on neuroinflammation and Alzheimer's disease

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Background

Exposure to early life stress (ELS) can determine long-lasting effects on the immune system, including its priming towards a pro-inflammatory state, and therefore impacting its function for the rest of the individual's life. These effects could also make the individual more susceptible to further stressors later in life, with the risk of triggering a chronic inflammatory response. When inflammation concerns the central nervous system, we talk about neuroinflammation, a key process in the development of multiple pathologies, like Alzheimer's disease (AD). As up to date, no disease-modifying therapies for AD are available; the focus on neuroinflammation as a therapeutic target has been increasing. In particular, the focus of this study is on TNF α , a cytokine involved in the inflammatory process with the capacity of binding two distinct receptors: TNFR1, which has pro-inflammatory properties, and TNFR2 with neuroprotective and anti-inflammatory activity. Promoting the activation of the latter represents a potential therapeutic strategy for a neurodegenerative disease such as AD.

Objective

The goal of this project is to set up a mouse model of combined early life stress, followed by chronic social stress (CSS) during adulthood, to evaluate the effect on neuroinflammation and on the onset, development, and progression of AD. Moreover, once the model is established, following the combined stress mice will receive a treatment with a TNFR2 agonist, to evaluate whether this intervention can ameliorate the AD phenotype both at a molecular and behavioral level.

Design/methods

Mice (both male and female, both AD models and wild type) will undergo two different stress protocols: the limited bedding and nesting paradigm will be used at an early stage for ELS, while the chronic social defeat paradigm will be used as CSS during adulthood. Control mice with no stress exposure will be included as well. Mice will then perform a battery of behavioral tests to evaluate memory and cognition. After that, molecular analyses will be conducted on their brain to evaluate markers of neuroinflammation and AD. Once the model is established, following the CSS mice will be treated twice a week for 6 weeks with a TNFR2 agonist, and then screened for the same behavioral tests and molecular analyses.

Conclusion

What we expect is to see an exacerbation of neuroinflammation and a worsening of AD pathology in mice exposed to ELS and CSS compared to those with no stress exposure. We also expect to see an improvement at both molecular and behavioral levels following the treatment with the TNFR2 agonist.

Using patient and sibling-derived iPSCs to investigate intrinsic astrocyte features that contribute to remyelination failure in multiple sclerosis

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Background

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system known to be debilitating for patients. Remyelination failure is a contributing factor to disease progression and can worsen symptoms. Postmortem MS astrocytes derived from white matter (WM) impair remyelination in *in vitro* myelinating cultures but have been exposed to a prolonged disease environment.

Objective

This adapted iPSC-to-iAstro differentiation protocol will be used to generate WM-like iAstro from hiPSCs derived from donors with primary progressive MS and their non-affected siblings and unrelated controls to compare injury-naïve MS and non-MS WM-like iAstro on both a biological and functional level with a focus on remyelination (failure).

Design/methods

To investigate whether MS astrocytes affect remyelination in an injury-naïve state, we used human induced pluripotent stem cell-derived (hiPSCs) astrocytes (iAstro). To generate injury-naïve WM iAstro, we first adapted a protocol published by Dittlau et al., by culturing the astrocytes in FBS-free medium supplemented with CNTF.

Results

The iAstro acquired a WM-like astrocyte morphology and expressed pan-astrocyte markers as detected by immunocytochemistry and western blot, while GM-like astrocyte markers GLT1 and GS were not detected.

Conclusion

Astrocytes are expected to play an important role in remyelination. In order to investigate MS and non-MS iAstro in a disease naïve state, we make use of iAstro derived from different disease status in order to uncover intrinsic astrocytic differences.

Assessment of Fitness to Drive in Patients with Early Parkinson's Disease including Assessment of Social Cognition and Risk-Taking Traffic Behavior

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Background: Previous studies have already demonstrated predictors of fitness to drive (FTDr) in patients with Parkinson's Disease (PD), such as motor symptoms, visual contrast sensitivity, and cognitive impairment. However, cognitive impairment plays an increasingly important role due to improved treatments for motor symptoms. Furthermore, cognitive impairment is already apparent before the onset of motor symptoms. Previous research dates from over 10 years ago and might not take recent advances and insight into account. An underexposed domain in FTDr in PD is social cognition (SC). SC impairments might influence fitness to drive through impaired decision-making processes

Objective: The aim of the current study was to assess predictors of fitness to drive in an on-road driving test in patients with early PD, including (social) cognitive functioning, motor performance and contrast sensitivity. Furthermore, we assessed the additional value of social cognition assessment for fitness to drive, in specific for risk-taking behavior in a driving simulator task.

Design/methods: Patients with PD were included between 35 and 60 months after diagnosis. Patients underwent neuropsychological assessment and a driving simulator task at the University Medical Center Groningen (UMCG), and an on-road test at the Dutch Driving Agency. First, point-biserial and spearman correlation analyses were performed between on-road driving assessment and motor symptoms (UPDRS-III), visual contrast sensitivity (Gecko), visual reaction times (Vienna S1), auditory reaction times (Vienna S2), divided attention (Vienna DT), mental speed (SDMT), visual perceptual speed/useful field of view (ATAVT), visuoconstructive functions (Rey Copy), Risk perception (AST-SWOV), and emotion recognition (FEEST). Significant predictors were included in a binomial logistic regression analysis, with the on-road driving test as outcome. Furthermore, associations between emotion recognition (sub)scores and risk-taking behavior in traffic (Swing SDLP, lateral swaying of the car caused lack of vehicle control due to high speed, and Inters-Viol, number of violations in an intersections drive) were analyzed with Pearson and Spearman correlations.

Results: Gecko, VTS DT, SDMT, TMT A en TMT B scores were significantly related to the on-road driving assessment and entered into the regression analysis. The logistic regression model was statistically significant, $\chi^2(5) = 14.963$, $p = .011$. The model explained 50.0% (Nagelkerke R²) of the variance, and correctly classified 89.7% of cases. Of the four predictor variables none were statistically significant. Regarding Social Cognition and risk-taking behavior, only recognition of surprise was significantly related to Swing-SDLP ($r_s = -.35$, $p = .039$).

Conclusion: The found prediction model for the on-road test is consistent with previous research, except motor scores were not predictive in our model. As we included patients with early PD (<5 year), motor symptoms might not be as pronounced yet or well controlled with medication. Contrary to what was expected, SC had little additional value in assessment of fitness to drive.

Deciphering white matter lesion evolution in multiple sclerosis through spatial microglial states

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Background

Multiple sclerosis (MS) is marked by focal demyelinating lesions that can be subclassified by their inflammatory profiles. Active lesions show widespread inflammation throughout the demyelinated lesion, while mixed active/inactive lesions are characterized by inflammation restricted to the rim of the lesion. Increasing evidence indicates that these lesions undergo evolution and transition to end-stage lesion types. Current work focuses on the importance of the spatial aspect of glial cells in MS lesions.

Objective

We aim to map transcriptomic signatures in lesion rims and cores and compare them to previously identified microglial states at single-cell resolution. This approach will help uncover spatially-resolved microglial phenotypes and their interactions with other glial cells across lesion types. Moving forward, we plan to expand to a more comprehensive analysis of glial crosstalk in MS pathology. We hypothesize that the transcriptional changes found in microglia lead to functional changes, which affect their immediate microenvironment and affect re- and de-myelination. Therefore, we aim to functionally disentangle the involvement of microglia states in processes underlying MS lesion evolution and decipher how distinct phenotypes affect remyelination.

Design/methods

Our research focuses on identifying transcriptomic patterns, particularly in microglia, across these lesion types using the 10x Genomics Xenium platform using a 366-gene panel. To investigate microglia states *in vitro*, we will differentiate iPSCs to microglia (iMicroglia). We will extrinsically induce iMicroglia states by exposure to CNS substrates, similar to the lesion microenvironment. The functional properties of various iPSC-derived glial cells and their respective states are investigated by co-cultures to recreate the MS-associated microenvironment. The functional aspects investigated are microglia-astrocyte interactions and myelination using various co-cultures.

Results

Currently, we are finishing our spatial transcriptomic data collection, where our lesion cohort consists of several active, mixed active/inactive, inactive, pre-active and remyelinated lesions, as well as several control tissues. Preliminary analysis shows a distinct transcriptomic pattern in which a different cluster of cells is found within and on the rim of mixed active/inactive lesions, indicating spatial microglial heterogeneity. The top markers of these different clusters resemble previously found markers for microglia specific for MS, which we will be trying to mimic *in vitro* using iPSC-derived microglia using CNS substrate exposure.

A1

Neural representation of male zebra finch songs in female CMM throughout pair bonding and tracking of their acoustic communication

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Background

Zebra finches (*Taeniopygia guttata*) are small, sexually dimorphic, socially monogamous birds that occur in Australia and the Lesser Sunda Islands of Indonesia. Males are vocal learners who learn to sing a tutor's song, while females learn to recognize the songs of their father or mate, but cannot sing themselves. However, both males and females are highly vocal and call frequently to communicate. Song is a large component of zebra finch courtship and shows important signals of male attraction. Females respond differently to a preferred familiar song over unfamiliar ones, which is thought to reflect memory. Secondary auditory regions, such as the caudomedial mesopallium (CMM), have been shown to be a key part in discriminating between hetero- and conspecific songs. Additionally, findings suggest that in females, the CMM may be (part of) the neural substrate for the representation of preferred songs, whether that is conspecific, female-directed, or father's song.

Objective

My main research question will be: How does CMM activity in females change over time throughout pair-bonding?

Design/methods

To observe how the CMM processes information throughout the pairbond, calcium imaging will be used. This will allow us to visualize real-time calcium-related activity of neurons in the CMM, acquiring a deeper understanding of the underlying neuronal processes involved in mate recognition and vocal negotiation. Additionally, behavioural responses to different songs will be observed for preference and interest. Furthermore, a bioacoustic camera will be used, which enables the detection of social communication in a complex socio-acoustic environment. This allows for the study of the female perception of male song and the development of pair bonding in a more ecologically relevant way.

Conclusion

I hypothesize that the activity of the CMM becomes more selective over time to its partner compared to other auditory stimuli.

This research will be the first study that considers the neural representation in the female CMM of male songs using calcium neuroimaging. The results gathered can be useful to better understand whether and how neural activity differentiates song identity, familiarity, and social context. This provides us with a fundamentally better understanding of what neural framework underlies mate choice/recognition, pair bonding and vocal negotiation.

A2

Brain Activation During a Hand-Force Task in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Comparing Baseline and Post-Exertional Malaise Conditions Over Two Days

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Background

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, debilitating multi-system disease with an unknown etiology. ME/CFS is characterized by sleep problems, “brain fog”, muscle and joint pain, and persistent and unexplained fatigue, which is not relieved by rest and is worsened by even mild exertion, characterizing its defining symptom: post-exertional malaise (PEM). PEM involves a delayed, disproportionate and worsening of the aforementioned symptoms triggered by even minor physical or mental efforts.

Functional MRI is increasingly used in ME/CFS research to explore brain networks involved in fatigue, cognition, and autonomic control, with growing numbers of task and resting-state studies showing altered activation patterns and connectivity that correlate with symptom severity.

Objective

The primary objective of my project involves analysing fMRI scans of affected and control participants while exploring within-patient and between-patient/group differences in brain activity during a specific hand-force task.

Design/methods

The project includes up to 100 participants: 50 people with ME/CFS and 50 controls matched at group level for age, sex, and activity. My role in this project will be focused on the analysis of the MRI data collected during physical tasks carried out over two consecutive days, namely the blood-oxygen-level-dependent (BOLD) activation at rest and during hand-force task – specifically the maximal voluntary contraction (MVC, 5 seconds) of the index finger abductor. I will perform pre-processing, first and second level analysis of these MRI scans.

Conclusion

It is hypothesised that task-based fMRI measures will differ between ME/CFS patients and controls, particularly on the second day after repeated cognitive and force tasks, when PEM is expected. In ME/CFS, this may include greater or more widespread brain activation reflecting recruitment of additional regions as a compensatory mechanism. Such insights could contribute to identifying objective neurobiological markers of PEM and inform the development of targeted interventions for ME/CFS.

B1

Biologically Inspired Continual Learning Through Synaptic Turnover and Self-Supervised Approaches

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Background

Biological brains learn continuously across the lifespan, integrating new experiences into memory, while keeping the ones that are already present intact. In contrast, artificial neural networks typically overwrite earlier knowledge when trained on new information. This problem is known as catastrophic forgetting. Existing computational strategies, such as synaptic intelligence, partially keep already learned knowledge but do not prevent the loss of plasticity, which is a problem that emerges when learning is prolonged. Recent studies suggest that reinitializing synaptic weights, which is considered to be similar to biological synaptic turnover, can restore plasticity without erasing previous learning. At the same time, self-supervised learning methods show that models can form rich, transferable internal representations without providing labels, making them promising candidates for lifelong adaptation.

Objective

This project aims to investigate biologically inspired mechanisms of continual learning by studying how synaptic turnover and self-supervised learning contribute to memory stability, plasticity, and representational change across sequential tasks. The hypothesis is that combining these mechanisms will provide better stability of learning across tasks while maintaining plasticity than current computational approaches.

Design/methods

Using computational modelling in Python and PyTorch, neural networks will be trained on sequential task paradigms implemented through the Avalanche library. Models incorporating synaptic turnover, continual self-supervised learning, and established baselines will be compared. Metrics will include catastrophic forgetting, forward and backward transfer, representational drift, linear readout performance, and resource usage, followed by statistical analysis.

Conclusion

This project will examine how synaptic renewal processes and self-supervised representation formation, both motivated by biological learning, contribute to long-term adaptability in artificial systems. The goal is to link neural mechanisms underlying lifelong learning with computational models that support continuous knowledge accumulation.

B2

The role of prefrontal brain waves in organizing working memory information domains

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Background: Working memory (WM) refers to the process of maintaining and manipulating behavior. It is essential to human cognition and acts as a sketchpad of conscious thought (Miller et al., 2018). The dorsolateral prefrontal cortex (DLPFC) has been identified to play a crucial role in WM and especially so in maintaining information (Owen et al., 2005). How the DLPFC manages the representation of information from different domains (i.e. visual, spatial, or verbal), or rather how they are organized, is not fully resolved.

One of the leading theories of how the brain communicates and shares information with other parts of the brain is the ‘communication by coherence’ hypothesis. It states that for two bodies of neurons to communicate successfully, their oscillatory patterns must match in a way that one of them spikes when the other one is ‘ready’ to receive input, i.e. during a certain phase of the relevant oscillation (Fries, 2005). When neural spiking occurs in synchrony with surrounding oscillations, we speak of spike-field coupling (SFC) (Buzsáki et al., 2012).

Animal studies have shown that the oscillation phase at which SFC occurs encodes information content in the hippocampus (Hafting et al., 2008), and theory suggests a possibly similar process for WM in the DLPFC (Owen et al., 2005; Fried et al., 2014; Kastner et al., 2007; Johnston & Everling, 2008).

Objective: The main hypothesis of the project is that the prefrontal theta oscillation organizes WM information from different domains. It is hypothesized that SFC at a specific (yet unknown) phase of the theta oscillation promotes WM performance in a certain domain (spatial, verbal or visual). In other words, we suspect that information from different domains is categorized into different phases of the theta oscillation in the DLPFC, and spiking during the relevant phase promotes recall in a certain domain. While we cannot non-invasively test SFC in humans, we can induce spiking at particular phases using transcranial magnetic stimulation (TMS) and electroencephalography (EEG). In the present study, we apply theta-phase specific stimulation. Given the proposed link between oscillation phase and memory, the TMS pulses are hypothesized to improve the performance of specific WM domains when TMS is applied at unique phases.

Design/methods: Participants will perform a delayed match to sample task where colored circles, with letters in them, are shown at different locations. After a retention interval, the participants are cued to which domain (color, spatial or verbal) they should respond. Another array of circles is then presented that is either the same as before or differs in exactly one of the domains. Participants must then indicate whether a change has occurred.

During the retention interval of the task, TMS will be applied to the DLPFC at 120% of the resting motor threshold of the participant. A MagStim Stimulator with a figure-of-eight coil will be used.

The participants will wear 64-channel EEG (electroencephalography) caps and EEG data will be recorded continuously during the tasks and analyzed in MATLAB.

Conclusion

This project will investigate whether the phase of the prefrontal theta oscillation organizes information from different domains in WM, using a delayed match-to-sample task, TMS and EEG.

C1

The impact of social interventions on the start and progression of Alzheimer's Disease

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Background

Reduced sociality across life is associated with an increased risk of brain disorders, including Alzheimer's disease (AD). Despite their heterogeneity, many neuropsychiatric disorders share social dysfunctioning, likely reflecting a common neural basis which arises from interactions between environmental factors and brain development. A potential neurobiological substrate of social dysfunction is the default mode network (DMN), which supports mentalizing and sociality. Disrupted DMN-FPN switching and DMN atrophy is associated with social deficits in AD. However, empirical evidence is missing on how social lifestyle influences AD pathology and which mechanisms are involved. Moreover, sex differences are also prominent in AD, with women showing higher prevalence and faster cognitive decline, indicating sex-specific vulnerability.

Objective

Current neuropsychiatric diagnostic frameworks are largely subjective and category based. This highlights the need for treatments grounded in a neurobiological basis rather than clinical presentation. This work aims to identify shared neurobiological mechanisms, which could inform transdiagnostic interventions and potentially benefit multiple conditions simultaneously. Additionally, despite AD being more prevalent in women, females remain underrepresented in AD research. Including both sexes is crucial for sex-specific disease mechanisms and advancing personalised treatment strategies. Therefore, preclinical manipulation of social behaviour across both sexes can clarify the directionality between neurocircuit dysfunction and social deficits.

Design/methods

Here, we will investigate whether social group size influences the start, character and progression of AD features. More specifically, male and female triple-transgenic (3xTg) mice will be subjected to an intervention period in which they will be housed in varying group sizes. The impact of this intervention on sociability, fear memory, and brain pathology will be assessed through behavioural assays and post-mortem brain analyses.

Conclusion

Early social interventions might delay the onset or mitigate AD-related phenotypes, potentially by reducing neurocircuit dysfunction in the default mode network (DMN) and its interactions with the frontoparietal network (FPN). Conversely, social isolation, such as single housing, may accelerate AD pathology. These effects could also manifest at the molecular level, including increased plaque load and neuroinflammatory markers. In triple-transgenic (3xTg) mice, females exhibit higher levels of social behaviour compared to wildtypes, whereas males show the opposite pattern, suggesting that males and females may differ in both vulnerability to AD pathology and responsiveness to social interventions. Together, this work seeks to establish social interactions as a modifiable, neurobiological factor in AD pathology, with implications for transdiagnostic strategies.

C2

The role of prefrontal theta oscillations in organizing the temporal order of items in working memory

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Background

Working memory (WM) supports the temporary storage and manipulation of information essential for complex cognition, yet its neural encoding mechanisms remain unclear. Evidence suggests that encoding may rely on spike–field coupling (SFC), whereby neuronal spiking is coordinated with ongoing neural oscillations. Studies in rodents show that spike timing relative to the oscillatory phase can encode spatial and sequential information. Given the role of theta oscillations in the dorsolateral prefrontal cortex (DLPFC), similar phase-specific SFC may underlie WM encoding in this region.

Objective

The objective of this project is to investigate whether the sequential order of items held in working memory is encoded by phase-specific neural activity relative to theta oscillations in the dorsolateral prefrontal cortex. Specifically, the study aims to test whether items presented at different serial positions are associated with distinct phases of the theta cycle.

Design/methods

To address this question, healthy participants will perform a sequential working memory task in which they memorize a series of numbers. Electroencephalography will be combined with transcranial magnetic stimulation to induce a proxy of SFC. TMS pulses will be applied during memory maintenance, and EEG will be used to determine the theta phase at which stimulation occurs. Working memory performance will be analyzed as a function of oscillatory phase and item position.

Conclusion

The findings of this project have the potential to advance our understanding of the neural mechanisms underlying working memory organization. Demonstrating phase-specific coding of sequential information would support oscillatory models of working memory and may inform future research and interventions targeting working memory impairments.

D1

Sex differences in the onset of cognitive deficit in TgF344 Rat Model of Alzheimer's Disease

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Background

Alzheimer's disease (AD) exhibits considerable sex differences, with women presenting faster hippocampal deterioration and a higher lifetime risk than men (Pinares-Garcia et al., 2018). However, females remain underrepresented in both AD and learning-memory research (Geller et al., 2018; Waters & Laitner, 2021). Task design further complicates interpretation, as males normally outperform females in spatial navigation tasks, which favour place-based strategies, whereas differences are diminished when reducing spatial demands (Yagi & Galea, 2018). Hippocampal-dependent processes are sensitive indicators of early cognitive decline in humans and rodent models (Yassa & Stark, 2011; Ally et al., 2015; Gephine et al., 2024). Touchscreen-based assays provide translational and strategy-independent alternatives, including the Trial-Unique Non-Matching to Location (TUNL) task, which assesses hippocampal-dependent spatial discrimination (Talpos et al., 2010). Despite extensive work in AD mouse models, sex-specific cognitive trajectories remain poorly defined in rat models.

Objective

This experiment aims to identify the age at which cognitive impairments emerge in the TgF344 Rat model of Alzheimer's Disease in males and females, as well as to assess whether these deficits appear earlier in one sex than the other.

Design/methods

The experiment will be conducted on both male and female adult TgF344-AD and wild-type littermate rats obtained at ~10–12 weeks of age. Two weeks after arrival, performance in the touchscreen apparatus will be motivated by food restriction. A week later, there will be a pretraining phase for habituation to the touchscreen. Then, the training phase will take place, during which rats will learn the touchscreen-based TUNL pattern separation task (ability to differentiate resembling spatial positions) and must reach a predefined performance criterion. Both phases will take place 5 times per week. Once rats reach criterion, the testing phase will be the next step. Female rats will undergo vaginal lavage immediately after testing sessions to monitor and control for potential effects of the estrous cycle. When testing is complete, tissues will be collected and analysed using immunohistochemistry to assess markers of AD pathology and synaptic plasticity.

Conclusion

Given the marked, but still underrepresented, sex differences observed in AD and learning-memory, further studying these differences will help identify the age at which cognitive impairments appear in the AD model and assess possible sex differences in the onset. Touchscreen-based assays will estimate hippocampal-dependent spatial discrimination.

D2

Effects of Esketamine in Wistar-Kyoto Rats on Circadian Rhythm

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Background

Circadian rhythm disturbances are a key feature of depressive disorders and are associated with disrupted sleep-wake cycles, altered activity rhythms, and dysregulated hypothalamic-pituitary- adrenal (HPA) axis function. The Wistar-Kyoto (WKY) rat, a validated model of depression, exhibits both HPA hyperactivity and altered circadian regulation. Esketamine, a rapid-acting antidepressant, has been shown to modulate core clock gene expression and shift circadian activity rhythms, suggesting that part of its therapeutic action may involve effects on circadian mechanisms.

Objective

This project aims to investigate how esketamine administration influences circadian locomotor activity rhythms in male and female Wistar-Kyoto rats under conditions that isolate endogenous circadian function.

Design/Methods

Male and female WKY rats will be individually housed under a 12:12 light-dark cycle with ad libitum access to food and water. After a 10-day acclimation and baseline activity recording, animals will receive either a single dose of esketamine or placebo and will be maintained in constant darkness for 10 days. Locomotor activity will be continuously recorded using infrared motion sensors. Female estrous phases will be determined by daily vaginal cytology to account for hormonal effects. Animal handling, behavioral recording, estrous cycle assessment, tissue collection, circadian rhythm analysis, and data interpretation will be performed.

Expected Results

Esketamine treatment is expected to alter circadian locomotor rhythms relative to controls, potentially reflected in changes in period length, activity phase, or rhythm amplitude. Both sexes are predicted to show circadian modulation, though effect magnitude may differ between males and females.

Possible Implications

Understanding how esketamine influences circadian regulation in a depression-relevant model may clarify neurobiological mechanisms underlying its rapid antidepressant effects. Demonstrating circadian modulation could inform optimal treatment timing and highlight the role of sex differences in antidepressant efficacy, supporting the integration of circadian biology into personalized psychiatric treatment strategies.

E1

A Gut feeling: Gut Microbiota-Derived Curli Proteins and Genetic Risk factors in Early α -Synuclein Aggregation in Parkinson's Disease

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Background

Parkinson's disease (PD) is the second most common neurodegenerative disease world-wide, and its incidence is growing. Despite the high burden of PD, much remains unclear about the pathological processes underlying PD. Increasingly, evidence has shown that the gut-brain axis plays an important role in PD risk and progression. A defining feature of PD pathology is aggregation of α -synuclein (α -syn). According to the "body-first hypothesis of PD", pathological α -syn aggregation originates in the enteric nervous system in the gut and subsequently spreads to the brain via the vagus nerve. Within the gut, curli producing proteins, such as *E.coli*, have been suggested to promote α -syn misfolding in enteric nervous cells through cross-seeding mechanisms. Gut microbiome alterations and α -syn aggregation are commonly observed in PD, however the disease likely develops in the presence of additional genetic and environmental risk factors, such as GBA1 mutations and pesticide exposure. While the gut-brain axis may play a critical role in the initiation and progression of PD pathology, the direct influence of genetic and environmental risk factors on aggregation of α -syn in the enteric nervous system has not been directly investigated.

Objectives

This project aims to assess the effects of curli producing bacterial proteins, in interaction with genetic and environmental risk factors, on α -syn aggregation in iPSC derived vagal neural crest cells (VNCCs). Specifically, the project aims to: (1) assess the impact of bacterial curli, produced by *E.coli*, on α -syn aggregation in VNCCs; (2) examine how genetic vulnerability modulates curli-induced pathology; and (3) explore whether the presence of beneficial commensal bacteria can mitigate curli-driven α -syn aggregation.

Design/Methods

Human iPSC-derived vagal neural crest cells from PD patients, with or without a GBA1 mutation, and healthy controls will be exposed to bacterial supernatants, either containing *E.coli* and/or beneficial commensals, like *R. inulinivorans*. α -Syn aggregation will be quantified in VNCCs using immunocytochemistry and biochemical assays, then the extent and pattern of α -Syn aggregation will be compared across all experimental groups to determine whether exposure to bacterial supernatants differentially modulates aggregation in patient-derived versus control cells.

Conclusion

If successful, the study will identify key mechanisms linking gut microbes to early α -syn pathology, enabling development of novel early biomarkers and gut-targeted strategies for PD prevention and therapy.

E2

Retrieving sleep deprivation-induced spatial memory amnesia in male and female mice using a PDE4 inhibitor, optogenetics, and memory engram technologies

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Background

Sleep deprivation (SD) severely impairs cognitive processes, including memory formation and consolidation. However, recent evidence suggests that forgetting may not result from information loss, but rather from difficulties in retrieving stored memories. This distinction is critical for developing therapeutic interventions targeting memory impairments. Furthermore, sleep loss affects neural plasticity, stress responses, and memory performance differently in males and females, making sex-dependent effects essential to understand for avoiding male-biased conclusions and identifying distinct mechanisms of sleep deprivation-induced amnesia.

Objective

This study aims to investigate whether SD-induced amnesia in an object-location memory task can be reversed in male and female mice using targeted optogenetic reactivation of memory engrams. Additionally, this approach will be used in combination with the phosphodiesterase-4 (PDE4) inhibitor roflumilast to restore the "lost" memories permanently.

Design/methods

This is an experimental wet-lab study using male and female C57BL/6J and c-fos-tTA transgenic mice. The protocol includes an object-location memory task followed by gentle sleep deprivation. Active memory engram cells will be tagged during encoding and subsequently reactivated using optogenetic light stimulation during retrieval tests. To assess persistent memory recovery, optogenetics is combined with pharmacological manipulation using systemic administration of roflumilast. cFos immunohistochemistry and fluorescent imaging are used to visualize and validate the reactivation of engrams.

Conclusion

This study is expected to demonstrate that SD-induced object-location memory impairments can be persistently restored, indicating a reversible retrieval deficit rather than permanent information loss. By combining the use of optogenetics and PDE4 inhibitors, this research highlights a novel translational strategy for targeting memory dysfunction. Additionally, by including sex as a biological variable, it aims to uncover key neural mechanisms underlying memory recovery that could guide future interventions for Alzheimer's disease and age-related cognitive decline.

F1

Expanding time with a change: How changing visual properties impacts time perception

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Background

Analogous to other modes of perception, time perception is subject to many illusions and distortions. One such distortion is the change bias – a tendency to overestimate the duration between two stimuli when a visual property changes between them. This bias has been attributed to a magnitude coding effect: a visual change elicits a stronger sensory response reflected in greater P2 amplitude. The greater sensory response and the associated lengthening of perceived duration likely arise in the parietal cortex, which has been identified as the locus of time, space, and quantity perception. Conversely, if stimulus properties remain constant, sensory neurons become less responsive due to repetition suppression, and as such, the perception of duration is less likely to be overestimated.

Objective

In this project, we will use EEG measures in a temporal reproduction task with visual changes and repetitions in different dimensions to identify the neural signatures of the change bias, linking behavioural effects to neural components such as the P2.

Design/methods

In the experiment, each trial of the reproduction task begins with a presentation of two stimuli separated by a variable interval, which will serve as a reference duration. Depending on the condition, a visual change will occur between the two stimuli, or the visual properties will remain constant. On visual change trials, the second stimulus could differ from the first either in its location, size or orientation. Thereafter, participants will reproduce the reference duration by pressing a key after the onset of a cue, responding only when they believe that the second stimulus should appear. Participants' EEG signals will be measured as they complete the reproduction task.

Results

Our primary prediction is that a change in size or location of the second stimulus will lead to the perception of greater temporal distance between the two stimuli. Furthermore, we anticipate that changing the size or location of the second stimulus will result in an increased amplitude of the P2 component. Conversely, a change in stimulus orientation should not lead to the change bias since neurons in the parietal cortex do not code for such dimensions.

Conclusion

By providing results in line with our hypotheses, we aim to elucidate the conditions under which time perception gets distorted, and to find out whether these distortions arise in the parietal cortex coding for properties of magnitude.

F2

Can Mindfulness Training Normalize Depression-Related Speech Features in At-Risk Individuals?

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Background

Depression is linked to characteristic speech alterations, including increased first-person singular pronoun use and negative emotion words, as well as reduced speech rate, reduced pitch variability, and increased pause frequency. Mindfulness-based interventions effectively reduce ruminative thinking in individuals at risk for depression, but their impact on speech features related to depression remains unknown.

Objective

This study will investigate whether a mindfulness intervention in individuals at risk for depression can alter linguistic and acoustic speech features toward patterns observed in less vulnerable individuals.

Methods

A Randomized Controlled Trial (RCT) will allocate participants to either the mindfulness intervention group or an active control group listening to poetry. Participants will listen to a 10-min daily practice through a pre-recorded audio over the course of two weeks. After each session, participants will record a 1-min audio in which they talk about how they are feeling on that particular day. Pre- and post-intervention tests will be conducted to measure the effects of the intervention on speech behaviors, which will be captured by asking participants to respond to brief, general prompts. Data analysis will consist of separate linear mixed-effects models (LME) for each speech feature, where each model will assess the group × time interaction as the primary indicator of intervention effects.

Results

This study aims at examining whether a mindfulness intervention could cause speech features to become more similar to those of individuals who are less vulnerable to depression. It is hypothesized that speech features commonly associated with depression will be reduced after completion of the 2-week intervention. Concomitantly, we expect that one single session of mindfulness training will also yield reductions in depression-linked speech features.

Conclusion

If confirmed, these findings would provide first evidence that mindfulness training modifies depression-linked speech features in individuals vulnerable to depression and would support these speech features as possible biomarkers of intervention effectiveness.

G1

Social-Support Figures Enhance Rather Than Protect from Fear Extinction: A Multi-lab Extended Replication Report

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Background

Exposure therapy is the fundamental treatment for anxiety and fear-related disorders, yet even after successful treatment, relapses and return of fear are common (Hofmann & Smits, 2008; Levy et al., 2021). Clinical guidelines typically recommend removing all safety signals, including social-support figures, during exposure. However, Hornstein et al. (2018) propose that social-support figures may be a distinct class of safety stimuli with prepared fear-inhibitory properties that differ fundamentally from learned safety signals. Notably, pairing conditioned threat cues with images of social-support figures during extinction has been shown to enhance extinction learning and attenuate return of fear, even after the social cues are removed.

Objective

The primary objective is to replicate and strengthen previous findings from Hornstein et al., (2018) study, which demonstrates that social-support figures enhance rather than protect from fear extinction. A second objective is to elucidate the mechanisms underlying these effects by investigating whether social-support figures affect explicit threat appraisal in addition to physiological indices of fear. A third objective is to examine whether individual differences in psychological traits, including trait anxiety, attachment style, distress tolerance, and self-efficacy, impact the effects of social-support figures on fear inhibition during extinction and follow-up.

Design/methods

The project utilizes a standardized protocol to conduct an experimental fear-conditioning paradigm across three different laboratories. Healthy adult participants will complete a laboratory session consisting of habituation, acquisition, paired-extinction, and return-of-fear test phases. During acquisition phase, two neutral visual stimuli (CS+s) will be paired with a mild electrocutaneous stimulus (unconditioned stimulus; US), whereas a third neutral stimulus (CS-) will serve as safety signal and will not be paired with the US. During paired extinction phase, each CS+ will be presented without reinforcement and paired either with an image of a participant-nominated social-support figure or with an image of a smiling stranger, and the CS- will be presented alone. During return-of-fear test, all stimuli will be presented alone (no US; no secondary images). Fear responses will be assessed using skin conductance responses, as well as trial-by-trial self-reported US-expectancy ratings. Brief psychological trait questionnaires will be administered to examine individual differences in the fear-inhibitory effects of social-support figures. Finally, a reinstatement procedure and follow-up test will be conducted 24 hours later.

Conclusion

The findings of this project have the potential to significantly expand both theoretical and clinical understanding of fear extinction. By conducting a multi-laboratory replication, this study will elucidate whether social-support figures will consistently facilitate extinction learning and reduce the return of fear. If confirmed, these findings may challenge prevailing assumptions about the detrimental role of safety signals during exposure therapy (Hermans et al., 2006) and enhance frameworks of inhibitory learning, relapse prevention and clinical guidelines.

G2

Predicting CBT Outcomes in Youth Anxiety: Cognition and Ethnicity in an IPD Meta-Analysis

Javier Garrido Jiménez

Background

Cognitive Behavioural Therapy (CBT) is an effective treatment for anxiety disorders in children and adolescents, yet treatment outcomes vary substantially between individuals. Progress in identifying predictors and moderators has been limited by underpowered single trials and inconsistent measurement across studies. Individual Participant Data Meta-Analysis (IPD-MA) offers a way to address these limitations through large-scale harmonization and pooled modelling.

Objective

This project examines whether cognitive characteristics and ethnicity-related variables predict post-treatment remission following CBT in youth anxiety, and whether these factors moderate CBT treatment effects across trials.

Design/Methods

Using the Platform for Anxiety Disorder Data in Youth (PADDY; ≈81 CBT-based trials; >7,000 participants aged 3–18), predictor variables will be systematically harmonized across studies. Ethnicity-related variables will be coded by minority status relative to each trial's national majority group. Cognitive predictors will focus on negative self-talk (NASSQ) and coping-related measures (CQC/CRI). Outcomes will be analysed using one-stage multilevel models accounting for clustering within trials. Primary analyses will test independent associations of ethnicity and cognitive predictors with remission, controlling for baseline severity, age, sex, and socioeconomic indicators. Moderation analyses will test whether these variables modify CBT effects relative to control conditions.

Conclusion

This study aims to clarify how socio-cultural and cognitive differences contribute to heterogeneity in youth CBT outcomes, supporting more personalized treatment allocation and demonstrating the value of harmonized IPD approaches in youth mental health research.

H1

Does Meditation Modulate Bayesian Temporal Inference

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Background

Time perception in the mind involves constructive inference, and not just a direct readout of physical time. In timing tasks, participants often show sequential effects (serial dependence), where current estimates are pulled toward recent experiences. This pattern fits Bayesian accounts, in which perception combines current sensory evidence with prior expectations and beliefs. A key feature of these Bayesian accounts is that the relative contribution of past and present is weighted by their reliability: when one is uncertain, reliance on the other increases. Meditation offers a way to test whether the internal state modulates this inferential process. Different practices can change attention stability, arousal, and meta-awareness, which may alter precision-weighting in perception. We believe this might thereby modulate the balance between prior context and current evidence in timing. Advanced meditators may therefore show meditation practice-dependent changes in sequential biases and the computational processes underlying temporal updating.

Objective

The first objective is to test whether meditation state changes how people estimate and reproduce short time intervals. The second objective is to quantify whether meditation alters reliability-weighted temporal updating (i.e., how much the system relies on recent history vs the current stimulus), using a Bayesian Kalman Filter model. And last to compare these effects across different meditation practices in advanced meditators.

Design/methods

Advanced meditators will complete multiple sessions/blocks in which they perform (i) two meditation practices and (ii) a control condition (e.g., quiet rest), each followed immediately by a time-perception interval reproduction task. The task presents brief intervals using a visual stimulus (Gabor embedded in noise), where stimulus reliability/precision is manipulated (e.g., high vs low signal-to-noise). The noise manipulation enables estimating how prior-trial information is weighted as a function of reliability. The data will be analysed using a Bayesian Kalman filter model.

Conclusion

This project can clarify whether meditation alters core computational mechanisms of perception, specifically how the brain weights sensory evidence versus prior context under uncertainty. More broadly, the work could motivate using timing tasks and Bayesian model parameters as sensitive behavioral markers of short-term state changes, with potential relevance for interventions targeting attention dysregulation (e.g., stress, anxiety) and for mechanistic evaluation of mindfulness-based training.

H2

In vivo calcium imaging to investigate the dynamics of neural responses underlying song memory in adult zebra finches

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Background

In male juvenile zebra finches, an auditory memory of an experienced tutor's courtship song is formed during their sensory plastic period for vocal learning (Yanagihara & Yazaki-Sugiyama, 2016, *Nat Commun*). During this time, these birds accurately reproduce the tutor song, ultimately forming a crystallized song by the closure of the plastic period (Louder et al., 2024, *Cell Rep*; Yanagihara & Yazaki-Sugiyama, 2016, *Nat Commun*). Research has suggested that the tutor song memory might reside in a secondary auditory region called the caudomedial nidopallium (NCM) (Bolhuis & Gahr, 2006, *Nat Rev Neurosci*; Bolhuis & Moorman, 2015, *Neurosci Biobehav Rev*; Hahnloser & Kotowicz, 2010, *Curr Opin Neurobiol*). Whereas research has studied the neural substrate of this memory in juveniles (Yanagihara & Yazaki-Sugiyama, 2016, *Nat Commun*), it is currently unknown how the neural substrate underlying song memory behaves in the NCM of adult zebra finches. Importantly, the neural dynamics underlying song memory in adult zebra finches have been investigated in the HVC, a premotor brain region (Katlowitz et al., 2018, *Neuron*; Liberti III et al., 2016, *Nat Neurosci*). These investigations have, however, provided contradicting results. Whereas Liberti III et al. (2016) reported drift in the neurons involved in a song memory over time, Katlowitz et al. (2018) rather observed the underlying activity patterns to remain stable.

Objective

The current project aims to elucidate the dynamics of the neural responses underlying song memory in the NCM of adult zebra finches over an extended period of time. Specifically, the project aims to determine whether the neuronal ensembles associated with song memory change over time, in accordance with the "neuronal drift hypothesis" (Mau et al., 2020, *eLife*), or whether the activity of these neuronal ensembles remains stable with time, in accordance with the "tuning constancy hypothesis" (Jensen et al., 2022, *Nat Neurosci*). It is expected that the neuronal substrate underlying song memory in the NCM will be dynamic over time, albeit to a lower degree given the consistent and stereotypical nature of a crystallized zebra finch song (Louder et al., 2024, *Cell Rep*).

Design/Methods

The neural dynamics of song memory will be assessed by playing manually recorded tutor songs and control stimuli to male adult zebra finches and subsequently recording and visualizing the neural responses through in vivo calcium imaging using one-photon microscopy. After obtaining these neural recordings, birds will be sacrificed and the brain material will be processed and visualized through immunohistochemistry analysis and fluorescence microscopy, respectively.

Conclusion

The findings of this project may provide insight into how tutor song memory is maintained in the adult zebra finch brain, specifically in the NCM region. Additionally, findings may provide additional evidence for the NCM as the site for storage of tutor song memory (Yanagihara & Yazaki-Sugiyama, 2016, *Nat Commun*). Lastly, zebra finches are a valuable translational model for human speech acquisition (Bolhuis et al., 2010, *Nat Rev Neurosci*; Yanagihara & Yazaki-Sugiyama, 2016, *Nat Commun*), with long-term goals concerning insights into speech development deficiencies in children.

Inhibiting behavior, inhibiting thoughts: a thought-probe stop-signal approach to sticky Mind Wandering and response inhibition

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Background

Mind Wandering (MW) is a well-documented phenomenon characterized by shifts of attention from an ongoing task to unrelated thoughts and feelings. This tendency is widespread across cultures and is estimated to occupy a substantial portion of waking time. Although MW episodes are known to impair task performance, their impact on executive functions remains insufficiently explored. Particularly, rigid and inflexible forms of MW, closely related to rumination, appear to produce the most detrimental effects on goal-directed behavior and mental wellbeing. Previous research demonstrated that MW disrupts the control of rapid behavioral action cancellation (i.e., response inhibition) by damaging the ability to trigger an 'inhibitory break'. Despite this, no studies have yet examined the plausible relation between response inhibition performance and the '*stickiness*' (i.e., difficulty to disengage from) of irrelevant thoughts.

Objective

The present study aims at investigating the relationship between recurrent and difficult-to-disengage-from forms of MW and response inhibition in healthy subjects. Possible cross-culture differences will also be explored through a collaboration with the Indian Institute of Technology Delhi, where the same experiment will be conducted.

Design/Methods

Participants will complete a computerized behavioral task, accompanied by the administration of questionnaires, such as the Perseverative Thinking Questionnaire (PTQ). The paradigm consists of a stop-signal task (SST), a validated measure of response inhibition, combined with thought-probes to assess both MW episodes and their '*stickiness*'. Within- and between-subject analyses will examine, respectively, performance differences between MW and on-task episodes and group differences related to the individual MW tendency.

Expected Results

In addition to replicating previous findings, it is expected that greater reported '*stickiness*' of off-task thought is associated with poorer task performance.

Possible implications

Both perseverative self-generated experiences and impaired response inhibition are associated with psychopathology and broader behavioral and health problems. Thus, clarifying how internally generated ruminant thought impacts high-order executive functions holds significant clinical value, particularly for the development of interventions such as Mindfulness-based trainings. Moreover, different everyday activities, including driving and operating machinery, require rapid response inhibition, highlighting the potential real-world relevance of these findings.

Keywords: Mind Wandering, Response Inhibition, Perseverative Thinking, Cross-Cultural Comparison

Effects of esketamine on circadian activity rhythms in Wistar–Kyoto rats

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Background

Disturbances in circadian rhythms are a hallmark of depressive disorders and are commonly reflected in disrupted sleep–wake cycles and altered daily activity patterns. The Wistar–Kyoto (WKY) rat is a well-established animal model of depression and displays abnormalities in both stress regulation and circadian rhythmicity (Birnie et al., 2022). Esketamine is a rapid-acting antidepressant whose effects extend beyond acute neurotransmission and may involve modulation of the circadian system. Experimental studies show that ketamine can directly influence core molecular clock mechanisms by altering CLOCK:BMAL1 activity and clock gene expression (Bellet et al., 2011), and can shift behavioral circadian rhythms depending on the timing of administration (Mihara et al., 2012). In clinical settings, ketamine-induced changes in circadian activity rhythms have been linked to antidepressant response (Duncan et al., 2017).

Objective

This project aims to examine how esketamine affects endogenous circadian locomotor activity rhythms in WKY rats. In addition, potential differences between male and female rats in their circadian responses to esketamine are explored.

Design/Methods

Male and female WKY rats are housed individually under controlled laboratory conditions. Locomotor activity is recorded using infrared motion sensors during an initial baseline period under a 12:12 h light–dark cycle. Rats then receive a single dose of esketamine or placebo and after this are kept in constant darkness for ten days to assess endogenous circadian rhythms in the absence of light cues. Changes in rhythm characteristics such as activity patterns, rhythm strength, and timing are analyzed. In female rats, the estrous cycle is monitored to account for hormonal influences during data analysis.

Conclusion

This study investigates the circadian effects of esketamine in a depression-relevant animal model. By characterizing changes in circadian activity rhythms and evaluating sex-dependent effects, the project may provide insight into how circadian regulation contributes to the antidepressant effects of esketamine. These findings could support the broader integration of circadian biology into research on rapid-acting antidepressant treatments.

J1

Dissociating gonadal and chromosomal sex effects on hippocampal-dependent spatial memory: modulation by artificial light at night

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Background

Sex differences in cognition arise from chromosomal and hormonal interactions, yet neuroscience often ignores sex as a biological variable or focuses on gonadal sex. The Four Core Genotype (4CG) model dissociates these by generating XX/XY mice with ovaries and testes. Hippocampal memory is sensitive to gonadal hormones, sex chromosomes and artificial light at night (ALAN), an increasingly important, potent circadian disruptor impairing hippocampal function. The Location Discrimination task enables the assessment of these interactions.

Objective

The main objective of this project is to dissociate between hormonal and chromosomal sex contributions to learning and performance, while exposed to ALAN, in the touchscreen-based Location Discrimination task using the Four Core Genotype mouse model. By independently assessing the effects of chromosomal sex and gonadal sex in combination with ALAN exposure, we aim to dissociate chromosome-driven and hormone-driven contributions to hippocampal sensitivity to ALAN.

Design/methods

In this project we will use Location Discrimination to assess hippocampal memory. Throughout all phases, the animals will be food-restricted to maintain 90% of their normal body weight. The animals will go through pre-training, training and trial phases. Once animals successfully complete the trial phase, they will transition to maintenance sessions. The ABET II software will be used to control the touchscreen chambers and automatically collect behavioral data. Each animal will perform the task once per day, five days a week, until placed on maintenance. Additionally, during the trial phase, we will monitor the estrous cycle daily. ALAN will be introduced in a randomized 50% of the mice during the trial phase.

Conclusion

ALAN is expected to reduce performance across all genotypes. Likely, ovary-bearing mice will show a bigger decrease compared to testes-bearing mice. XX-mice will be more sensitive to the decrease than XY-mice. Yielding lowest performance in XX-ovaries, highest in XY-testes, and intermediate in XX-testes and XY-ovaries. The ovary-bearing mice are expected to show greater deficits during the low-estrogen phase compared to the high-estrogen phase. This project will provide highly relevant information for the 4CG mouse model, enabling research that separates chromosomal from hormonal influences on learning under ALAN, a ubiquitous modern disruptor that impacts circadian and cognitive health. Ultimately, this work contributes to more precise modelling of sex differences in neuroscience research.

J2

Gating of social experience by the circadian clock in *Drosophila melanogaster* females

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Being in the presence of others impacts how an individual reacts to its environment. For example, when alone, an animal might spend less time feeding because it is alert to predators. However, in a group, the same animal may feed longer and stay calmer, thanks to shared vigilance. Although group living clearly benefits individuals, little is known about how the presence of others influences an individual's behavior and physiology. This project addresses this fundamental gap by investigating how social cues are integrated with environmental signals in the brain to modulate behavior and physiology, using the genetically tractable model organism *Drosophila melanogaster*. We recently discovered that light suppresses egg-laying in isolated female flies, but this inhibition is overridden in the presence of others an effect mediated by visual detection of conspecifics and integration of sensory cues via a neurohormonal pathway involving Juvenile Hormone. Our hypothesis is that neurons that sense the presence of others share circuits with those detecting light, letting social experience reshape how an individual perceives and adapts to its environment. We will test this by dissecting the neuronal and hormonal pathway that enables social context to modulate the effect of light on reproductive behavior. Our approach leverages the unparalleled genetic tools and complete female brain connectome available in *Drosophila*, allowing us to investigate this process with circuit-level precision. The project comprises three work packages: (1) identifying sensory neurons that detect light and social cues; (2) defining the neuronal circuits that integrate these inputs; and (3) mapping the hormonal and motor outputs that regulate egg-laying in response to these combined cues. This research will uncover how social context is sensed and transformed into specific physiological and behavioral responses, providing a comprehensive mechanistic framework for how social context affects an individual, from sensory input to behavioral output. Understanding how the presence of others reconfigures brain function and hormonal signaling will advance the biological basis of social influence on health, paving the way for novel insights into the benefits of social connectivity.

K1

The Prefrontal 'Switch': Distinguishing the Computational Role of the dlPFC in Decision-Making under Second-Order Uncertainty

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Background

Daily life is marked by uncertainty: from deciding whether to carry an umbrella to physicians choosing treatment for a patient. In some uncertain situations, we can predict the probability of outcomes, referred to as 'first-order uncertainty', or risk. However, sometimes outcome probabilities cannot be accurately computed, known as 'second-order uncertainty'. Second-order uncertainty arises from two sources: contingency ambiguity, where the information required to determine the outcome probabilities is missing, and contingency volatility, where outcome probabilities change over time. While research suggests a link between the dorsal anterior cingulate cortex and general second-order uncertainty, evidence also points toward a functional dissociation within the prefrontal cortex. Following Gläscher et al. (2012) lesion-mapping work, adaptive behaviour relies on partially dissociable prefrontal networks: a medial valuation system and a lateral cognitive control system. Given evidence for the involvement of the dorsolateral prefrontal cortex (dlPFC) in learning rate changes and medial prefrontal regions in ambiguity aversion, the different forms of second-order uncertainty may be supported by partly distinct prefrontal circuits.

Objective

We aim to causally distinguish the neural processing of contingency ambiguity and contingency volatility using non-invasive brain stimulation. By stimulating the dlPFC during decision-making computations involving both forms of second-order uncertainty, we seek to determine whether it supports strategy updating rather than uncertainty valuation. We predict that dlPFC stimulation will modulate the learning rate in volatile environments, reflecting its role as a computational 'switch', with a significantly smaller effect on ambiguity aversion.

Design/Methods

In a within-subjects, sham-controlled design, participants will receive excitatory tDCS over the left dlPFC during a reversal-learning task and a classic Ellsberg urn task to assess volatility and ambiguity, respectively. Behaviour will be analysed using adapted reinforcement learning and valuation models to isolate the learning rate (α) and ambiguity aversion (β) parameters. Reward sensitivity will be controlled for using the Sensitivity to Reward and Punishment Questionnaire.

Conclusion

By causally dissociating contingency ambiguity and contingency volatility, this study could further clarify the organisation of second-order uncertainty in the prefrontal cortex. Uncovering the dlPFC as a switch for volatility, distinct from medial valuation processes, could inform models of disorders marked by cognitive inflexibility.

K2

Investigating the therapeutic efficiency of TNFR2 agonist treatment in the EAE mouse model for multiple sclerosis

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Background

Multiple sclerosis (MS) is an autoimmune disease characterized by inflammation and demyelinated lesions in the central nervous system (CNS), leading to motor, sensory, and cognitive deficits. The cause of MS is not fully understood and there is currently no cure. An increase in tumor necrosis factor-alpha (TNF- α) is seen in active and chronic active MS lesions. TNF- α is a pro-inflammatory cytokine involved in many inflammatory diseases, including MS. TNF- α binds to tumor necrosis factor receptor 1 and 2 (TNFR1 and TNFR2). Binding to TNFR1 results in pro-inflammatory functions, while binding to TNFR2 is associated with immune modulation and tissue regeneration. Therefore, TNFR2 is a promising therapeutic target for MS treatment. One of the animal models for MS is the experimental autoimmune encephalomyelitis (EAE) mouse model. Studies show that systemic administration of a TNFR2 agonist alleviates peripheral and central inflammation, and reduces demyelination and neurodegeneration in female EAE mice.

Objective

This study aims to investigate the therapeutic efficiency of a specific TNFR2 agonist treatment in the EAE mouse model for MS.

Design/methods

This will be investigated by injection of TNFR2 agonist or a vehicle in male and female mice. The motor function will be scored and the Von Frey test will be done to measure mechanical allodynia. The mice will be sacrificed and the brain, spinal cord, lymph nodes, spleen, sciatic nerve, blood and CSF will be taken for examination. Immunohistochemical staining will be performed to examine neuroinflammation, immune infiltration, and demyelination. In addition, ELISA will be done to measure the neurofilament light chain (NfL) marker.

The hypothesis is that the TNFR2 agonist treatment will cause an immune modulatory effect, resulting in less inflammation compared to the control group. It is expected that the TNFR2 agonist treated mice have better motor function and have a higher threshold in the Von Frey test. Additionally, it is expected that the immunohistochemical staining shows less neuroinflammation, less immune infiltration, and less demyelination in TNFR2 agonist treated mice compared to the control group. Furthermore, it is expected that ELISA results will show less NfL marker in TNFR2 agonist treated mice compared to the control group.

Conclusion/implication

The findings will contribute to the understanding of TNFR2-mediated immune modulation, and positive outcomes of this study will support the therapeutic targeting of TNFR2 in MS treatment. Furthermore, this could pave the way for clinical trials, potentially offering a novel MS treatment. In addition, TNFR2 agonist treatment might also be efficient in other neuroinflammatory diseases, such as Alzheimer's disease or Parkinson's disease.

L1

Determining Sex Chromosome and Gonadal Hormone Influences on Pattern Separation in a 4CG Mouse Model

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Background

Biological sex differences are defined by both gonadal hormones and sex chromosomes. Both factors are known to influence the brain both during development and after birth, leading to differences in behaviour between males and females. One example of this is hippocampus-dependent tasks, where males typically outperform females. This observation is often attributed to the activation effects of gonadal hormones, while sex chromosome effects are largely understudied. Mouse models are often tested for hippocampal memory with tasks relating to navigation, which is not the standard for humans. A task with higher translational value has been developed to assess pattern separation capabilities in mouse models, a process associated with the dentate gyrus of the hippocampus.

Objective

The objective is to investigate sex differences in pattern separation, as measured by performance in a Touchscreen-based Location Discrimination (LD) task. A secondary goal is to dissociate the effects of hormonal and chromosomal sex through the use of the 4CG mouse line.

Design/methods

To investigate how sex hormones and sex chromosomes independently influence behaviour, the four core genotype (4CG) mouse model is utilised. This model utilises a translocation of the Sry gene to generate four genotypes of mice, with either congruent (XX with ovaries, XY with testes) or incongruent (XX with testes, XY with ovaries) gonadal and chromosomal sex. A previously established lab protocol is used to train the mice and then complete the behavioural testing on the touchscreen-based LD task. Data collection will be recorded using ABET II cognition software. The main outcome measure will be performance in the pattern separation task. Additionally, during the trial phase, the stages of the oestrous cycle will be monitored in mice with ovaries through vaginal lavage sampling to monitor hormonal influences on behaviour.

Conclusion

To fully understand how sex impacts behaviour, it is vital to independently study the impacts of sex hormones and sex chromosomes. The dentate gyrus is a key hippocampal region in memory consolidation, and researching it through pattern separation allows for a more comprehensive understanding of how biological sex can impact hippocampal memory functions. Based on the literature, we expect that standard males will outperform standard females, and mice with testes will outperform those with ovaries.

L2

Retrieving sleep deprivation-induced amnesia in social memory in male and female mice using a PDE4 inhibitor, optogenetics, and memory engram technologies

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Background

Sleep deprivation (SD) disrupts hippocampal-dependent memory processes, leading to consolidation failures and retrieval deficits. Recent studies suggest that while memory traces may persist, SD can make them temporarily inaccessible, highlighting the potential for reversible interventions. An important but underexplored area is social memory, essential for recognizing and responding to conspecifics. SD has been shown to cause long-term impairments in social recognition memory, indicating that sleep loss can obscure socially relevant memories. Additionally, SD affects memory performance differently in males and females, making sex a crucial factor in understanding these mechanisms. This project will investigate SD-induced deficits in social recognition memory in both sexes, addressing a critical gap in understanding how sleep loss differentially affects social memory accessibility across males and females.

Objective

The study aims to determine whether “lost” social memories can be recovered in male and female mice through targeted optogenetic reactivation of memory engram cells, alone or combined with the phosphodiesterase-4 (PDE4) inhibitor roflumilast. This directly tests the retrieval-deficit hypothesis in a social memory context while assessing sex-dependent differences in memory recovery.

Methods

This study utilizes a wet-lab experimental approach using male and female C57BL/6J and c-fos-tTA transgenic mice. The protocol involves a social recognition memory task followed by gentle SD. Active memory engram cells are tagged during encoding and subsequently reactivated using optogenetic light stimulation during retrieval tests. Pharmacological manipulation is conducted using systemic administration of roflumilast combined with optogenetics to assess persistent memory recovery, while cFos immunohistochemistry and fluorescent imaging are used to validate the reactivation of engrams.

Conclusion

This research is expected to demonstrate that SD-induced social memory impairments represent a reversible retrieval deficit rather than permanent data loss. By validating the combined use of optogenetics and FDA-approved PDE4 inhibitors, this project highlights a novel translational pathway for treating memory dysfunctions. Moreover, by incorporating sex as a biological variable, the findings will provide critical insights into the neural mechanisms of social memory recovery, potentially informing future therapies for Alzheimer’s disease and age-related cognitive decline.

M1

Neurorepresentation of the zebra finch songs in females' secondary auditory areas throughout pairbonding and tracking of their acoustic communication

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Background

Zebra finches are small, granivorous, sexually dimorphic, and **socially monogamous** birds. They are highly social and vocal, but only male counterparts produce songs with **unique individual motifs**. Although song is not the only component of zebra finch **courtship**, it conveys important signals during female mate choice. Songs begin with a few introductory notes followed by a variable number of motif repetitions. They are learned through vocal learning processes (Catalano, I. & Woolley, S.C., 2025). The **caudomedial mesopallium (CMM)** is one of the brain regions involved in the processing of conspecific vocalizations; it is thought to store characteristics of the father's song and to permit later shaping of mate preferences in females (Avey et al., 2005).

Objective

The aim of this project is to understand how CMM activity in females reared in captivity differs when they are exposed to different stimuli, and specifically, how exposure to wild songs differs from exposure to songs produced by males reared in captivity in terms of neural activation.

Design/methods

To achieve this, a **calcium neuroimaging** approach will be adopted. The region selected for observation is the CMM. **Adeno-associated viral (AAV) vectors** will be injected to induce the expression of ultrasensitive genetically encoded calcium indicator proteins (GCaMP6). To observe neural activity, a miniature microscope and lenses will be implanted on the scalp of the birds. In individuals in which expression is successful, it will therefore be possible to observe **real-time, calcium-related neural activity** during the playback of different acoustic stimuli. This analysis will help elucidate the neural mechanisms underlying the formation of partner preference and how these processes are reflected in patterns of CMM activation (Graber et al., 2013). At the same time, a **bioacoustic camera** will be used to monitor the development of pair bonding and duetting behaviours (Anisimov et al., 2014). In parallel, **behavioural observations** will be conducted to assess whether the bird remains still or moves while listening to the acoustic cues.

Conclusion

This will be the first time that a calcium imaging approach is applied to the study of CMM activity. Therefore, any observations will provide fascinating **insights into the neural activity** of females during the formation of pair bonds. Throughout the study, **behavioural responses** will be analysed in conjunction with neural data to determine whether behavioural patterns overlap with, or differ from, what is suggested by the neuroimaging results.

M2

Sex Differences in the Effect of Chronic Sleep Deprivation on Hippocampal Dependent Memory in Rats

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Background

Sleep is essential for hippocampal-dependent learning and memory (Rasch & Born, 2013; Squire, 2009). Sleep loss disrupts these functions: short periods of deprivation impair long-term and working memory and reduce markers of synaptic plasticity (Havekes et al., 2016; Hagewoud et al., 2010; Xie et al., 2015). Chronic sleep restriction (CSR) similarly impairs memory and hippocampal function in rodents (Deurveilher et al., 2015), yet how these effects differ between males and females remains largely unknown. This gap is critical, as growing evidence shows that sleep and memory processes are not the same across sexes. This highlights the importance of incorporating sex as a biological variable when examining how CSR impacts cognition.

Objective

This project investigates sex differences in the consequences of CSR on hippocampal-dependent memory using a touchscreen task. The aim is to determine if deficits on touchscreen tests are induced by CSR and if they are more severe in one sex than the other.

Design/methods

Adult TgF344 wild-type rats (males and females) will be trained on a touchscreen-based pattern separation task. Once criterion is reached, rats will begin the CSR protocol. Weekly touchscreen testing will be performed to determine when a decline in performance emerges relative to criterion. Female rats will undergo vaginal lavage after testing to monitor the oestrous cycle. When a performance impairment is detected, tissues and blood will be collected for biochemical analyses.

Conclusion

This project will clarify how CSR affects cognitive function in both males and females, addressing a major gap in sleep-memory research. Identifying sex-specific susceptibilities could improve the interpretation of behavioural studies that traditionally generalise across sexes. These findings may have implications for the development of more targeted strategies for treating cognitive deficits caused by sleep deprivation and inform experimental design in neuroscience by emphasising sex as a biological variable.

N1

Turning up the clock: inducing accelerated aging in human brain organoids

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Background

Brain organoids are a three-dimensional culture system composed of induced pluripotent stem cells (iPSCs). Their capacity to form complex networks resembling a developing human brain, along with the ability to easily manipulate cell genome in the lab, poses a powerful way to study the brain in vitro. Despite those advantages, organoids do not reach maturity, with most cells corresponding to the developmental stage of the first or second trimester. Aging is one of the key risk factors for many neurodegenerative diseases, including Alzheimer's and Parkinson's disease; thus, the absence of aging hallmarks poses a great limitation for modeling age-related pathologies. Induced aging has been successfully achieved in iPSCs by down-regulating progeroid genes (genes of hallmarks of aging), specifically mitochondrial polymerase gamma (Poly); however, this approach has not yet been translated to brain organoids.

Objective

This project aims to induce accelerated aging in brain organoids by establishing a robust down-regulation of Poly using clustered regularly interspaced short palindromic repeats interference (CRISPRi).

Design/methods

Poly knock down iPSCs achieved by CRISPRi will be used to culture organoids. Stability of the single guide RNA (sgRNA) construct in organoids will be tested with fluorescence-activated cell sorting (FACS). The effectiveness of doxycycline, given at various times and durations, will be established using quantitative polymerase chain reaction (qPCR), and various stainings. If feasible, the effect of Poly knock down will be investigated with qPCR or stainings.

Conclusion

This research aids in establishing a reliable method to accelerate aging in brain organoids, creating a model that can more accurately resemble the physiology of neurodegenerative diseases. Such advancements bring possibilities for a more precise understanding of late-onset disease progression and its underlying mechanisms, thus supporting the discovery of novel therapies for currently untreatable diseases such as Alzheimer's disease.

N2

Wait... What? Uncovering Learned Motor Inhibition in Temporal Preparation

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Background

We spend more time preparing than we might realize. For example, when waiting for the elevator, we rely on an internal sense of how long it will take before we should start moving again. This process, known as temporal preparation, describes how the brain anticipates the timing of upcoming events in order to optimize responses. Temporal preparation is often studied by manipulating the interval between a warning cue and a target stimulus, known as the foreperiod, with different cues predicting either predominantly short or predominantly long intervals. Findings suggest that both trial-level and prolonged preparation effects arise through associative learning. Computational modelling using the Formalized Multiple Trace Theory of Temporal Preparation (fMTP) framework proposes that these effects reflect a dynamic interplay between motor activation and inhibition, shaped by memory traces. In this view, temporal preparation emerges as a learned mapping between temporal units and motor inhibition or activation.

Objective

While the fMTP model successfully describes temporal preparation effects, direct evidence for its proposed neural mechanism is still needed. We aim to address this gap by directly testing whether the systematic manipulation of foreperiod frequency will induce associative learning that correspondingly modulates motor inhibition. For this, we will use Transcranial Magnetic Stimulation (TMS) to measure corticospinal excitability and inhibition during a variable foreperiod task.

Design/Methods

The experiment consists of an acquisition phase, followed by a transfer phase to test learning. Participants will complete a temporal preparation task, in which they perform a speeded key response when an imperative target stimulus is presented. Two different warning stimuli will be paired with either an exponential (predominantly short foreperiods) or anti-exponential (predominantly long foreperiods) distribution. Just before the shortest foreperiod, paired-pulse TMS will be applied, while electromyography will record motor-evoked potentials. This will allow us to probe the activity of two cortical inhibitory networks that are fundamental to motor control.

Conclusion

We expect decreased inhibition after the cue predicting short foreperiods. Conversely, the cue predicting long foreperiods should elicit stronger active inhibition at the same early point to prevent premature responding. For both reaction time and inhibition, we predict that cue-specific differences will be learned during acquisition and persist into the transfer phase.

O1

How does the framing of identical probabilistic outcomes as gains or losses affect neural reward prediction error signals (FRN/RewP)?

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Background

Human decision making is strongly influenced by whether outcomes are framed as gains or losses. Behavioural research has shown that losses tend to have a greater psychological impact than equivalent gains, a phenomenon commonly referred to as loss aversion. At the neural level, outcome evaluation can be studied using feedback locked EEG components such as the feedback related negativity (FRN) and the reward positivity (RewP), which reflect how outcomes deviate from expectations. However, it remains unclear how these neural prediction error signals differ when identical probabilistic outcomes are framed as gains versus losses.

Objective

The objective of this study is to examine how framing identical probabilistic reward outcomes as gains or losses influences neural reward prediction error signals. Specifically, the study aims to compare feedback related EEG components (FRN and RewP) caused by equivalent outcomes across gain and loss contexts while keeping outcome probabilities and expected value constant.

Design/ methods

Participants complete a two-part probabilistic decision-making task. In both parts, they repeatedly choose between three visual options associated with different outcome probabilities (70%, 50%, 30%) and proportional reward point amounts that yield identical expected final value. In the first part, outcomes are framed as reward gains, whereas in the second part the same outcomes are framed as reward losses. Participants receive immediate feedback after each choice. EEG is recorded continuously throughout the task. Analyses focus on frontocentral electrodes, where feedback related components are most prominent. FRN and RewP amplitudes are compared across gain and loss frames to assess how framing influences neural prediction error processing.

Conclusion

This study aims to provide insight into how outcome framing shapes neural prediction error processing. By directly comparing feedback related EEG responses across gain and loss contexts, the project seeks to clarify whether equivalent outcomes are evaluated differently at the neural level.

O2

Tossing and Turning: Investigating Sex Differences in Brain Aging and Cognitive Function Related to Sleep Disturbance at Midlife

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Background

Female sex is a biological risk factor for the development of Alzheimer's Disease (AD), reflected by greater lifetime risk and greater neural pathological markers. Relative to men, women experience greater burden for neurodegenerative pathology and more rapid cognitive decline. This might be due to women responding more poorly to sleep disturbance. Sleep disturbance during midlife is a risk factor for later dementia and among those with poor sleep, older women experience poorer outcomes for both cognition and brain volume. Importantly, midlife sleep disturbance is experienced by more than half of postmenopausal women. Given that sleep plays an important role in maintaining brain health, its disruption may contribute to the development of AD. The combined contribution of sleep disturbance and female physiology on AD risk related to reduction in brain volume and cognition, however, remains unexplored.

Objectives

The aim of this study is to investigate whether sleep affects brain aging and cognition differently in men and women at midlife and if this is affected by menopause status. Following a stepwise manner, this study will investigate 1) if brain aging and cognition at midlife is different between women and age-matched men, 2) if brain aging and cognition are different for good and bad sleepers and 3) whether sex and menopause status interact with sleep to influence brain aging and cognition at midlife.

Methods

This study will use data from several hundred midlife adults (age 40 to 60) of the UK Biobank cohort database. Multivariable linear regression models will be used to study the differences in brain aging and cognition between women grouped by menopause status and age-matched men, between good and bad sleepers, and how sex and their menopause status interacts with sleep to influence brain aging and cognition. Brain aging is measured using the Brain Age Gap proxy. This is derived by extracting grey- and white-matter volumes from the T1-weighted MRI scans, using a gradient boosting algorithm to predict the age of the brain and calculating the difference between brain and chronological age. Results from cognitive function tests will be used as measures of cognition. Actigraphy data of up to seven days per individual will be used to derive objective sleep measures. The regression models will control for age, subjective report of sleep quality and mood.

Conclusion

The results of this study could help link sleep disturbances experienced during menopause to vulnerability for AD, due to its effect on brain health and cognition. By better understanding this relationship, these findings could help to develop fitting treatments aimed at reducing sleep disturbance during menopause and thereby decrease the risk for AD.

P1

Effects of Glycation on an Alzheimer's Disease Blood-Brain Barrier Model

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Background

The brain is a highly metabolic organ that relies primarily on glucose to meet its energy demands (Mergenthaler et al., 2013). To support this metabolism while protecting neural tissue from harmful circulating factors, the blood–brain barrier (BBB) tightly regulates molecular transport between the blood and the brain (Rosenberg, 2012). Disruption of BBB integrity has been widely reported during ageing and in neurodegenerative disorders, including Alzheimer's disease (AD), where increased permeability is associated with neuroinflammation and disease progression (Montagne et al., 2017; Sweeney et al., 2018; Zenaro et al., 2017).

While glucose is essential for brain function, glycolysis also generates reactive by-products such as methylglyoxal (MGO). MGO is a highly reactive dicarbonyl compound that can induce glycation and has been shown to negatively affect multiple BBB components, including endothelial cells and pericytes, leading to oxidative stress, inflammatory signalling, and loss of barrier integrity (Berends et al., 2023). Ageing and AD are characterised by chronic metabolic stress and reduced cellular plasticity, which may limit the BBB's capacity to adapt to glycation-induced damage.

Objective

The objective of this project is to investigate the effects of glycation-induced metabolic stress on BBB properties in an *in vitro* model, with a specific focus on an Alzheimer's disease-relevant cellular context.

Design/methods

An *in vitro* collagen-based blood–brain barrier model will be exposed to methylglyoxal-induced glycation to simulate metabolic stress. The model will incorporate endothelial cells and iPSC-derived pericytes, including Alzheimer's disease-relevant cell lines. Barrier integrity will be evaluated using fluorescence imaging, immunocytochemistry, and quantitative PCR.

Conclusion

This project is based on the hypothesis that glycation-induced metabolic stress compromises blood–brain barrier integrity more strongly in an Alzheimer's disease-relevant cellular context, due to reduced cellular plasticity and stress resilience. By investigating glycation effects on BBB structure and molecular markers, the study aims to provide insight into disease-specific mechanisms underlying BBB dysfunction. The results may help clarify how metabolic stress contributes to barrier breakdown in neurodegeneration and could inform future strategies aimed at preserving or restoring BBB integrity in Alzheimer's disease.

P2

Digital memory screening in neurodegenerative disorders: validation and user experience of the Seattle–Groningen Memory Assessment (SGMA)

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Background

Neurodegenerative and neurological disorders are frequently associated with cognitive changes that are subtle, heterogeneous, and difficult to capture using traditional neuropsychological assessments. Standard cognitive tests including Mini Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA), are often limited in their sensitivity, repeatability, and suitability for frequent or remote assessment. Recently, digital, model-based cognitive assessments have been proposed as a promising alternative, as they allow for fine-grained measurement of cognitive processes and may provide clinically relevant parameters beyond total test scores. The Seattle-Groningen Memory Assessment (SGMA) is a brief, adaptive digital memory test that estimates individual memory parameters based on response accuracy and timing and has demonstrated good discriminative validity in previous research.

Objective

The aim of this study is to evaluate the usability and validate the Seattle–Groningen Memory Assessment (SGMA), in clinical neurological populations, including Parkinson’s disease and multiple sclerosis. Specifically, the study examines user experience (ease of use, clarity, and perceived burden), assesses the reliability of SGMA-derived parameters across repeated measurements, and evaluates the discriminative validity of the SGMA between healthy controls and clinical groups.

Design/methods

This study will use data from five groups; healthy older adults (50–80 years), individuals with MCI, early-stage dementia, Parkinson’s disease, and multiple sclerosis. Approximately 150 participants per group will be included. Participants will complete a digital memory assessment (SGMA) designed to estimate individual-level cognitive parameters based on performance accuracy and response timing. Where available, these parameters will be compared to baseline neuropsychological test outcomes and relevant clinical characteristics. Statistical modeling approaches will be used to examine associations between the digital parameter and clinical measures, as well as to explore potential subgroup differences.

Conclusion

By focusing on model-derived parameters from the SGMA, this study aims to contribute to the evaluation of digital cognitive assessments as tools for sensitive and scalable measurement of cognitive functioning in neurological populations. The findings may inform the potential integration of SGMA-based measures into both research and clinical practice.

Q1

When Equal Outcomes Feel Risky: P3b EEG Signatures of Probability-Based Risk Perception

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Background

Risk perception is a central determinant of risk-taking behavior, often independent of objective outcome probabilities. This is particularly relevant in gambling contexts: although lotteries are commonly perceived as low risk due to low stakes and salient potential gains, other gambling formats with identical expected values are often judged as substantially riskier. Although risk arises when potential consequences are combined with uncertainty, its subjective weighting varies across individuals.

Objective

The present de novo study investigates how risk perception differs between individuals and whether it is modulated by self-perceived riskiness and by the structure of gain versus loss environments.

Design/methods

To empirically assess risk perception, participants perform a probability learning task with three choice options in either a gain-only or a loss-only environment. Across both environments, all options are statistically equivalent in terms of expected value but differ in outcome structure: (1) high-frequency outcomes with low gains or losses, (2) moderate-frequency outcomes with random chance for either gains or losses, and (3) low-frequency outcomes with high gains or losses. Neural correlates of risk perception are examined using EEG, focusing on the risk prediction error as indexed by the P3b component.

Conclusion

By dissociating objective outcome statistics from subjective outcome structure, this study aims to elucidate how individuals perceive and evaluate risk beyond expected value, and how these processes are reflected in neural markers of outcome evaluation.

Q2

It's Dangerous to Go Alone: Gene by Social Environment Interaction in Determining Reproduction Decisions in *Drosophila Melanogaster*

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Background

The presence of others has profound influences on an individual's biology. Understanding the mechanism by which social interaction impacts an individual's physiology and behavior is therefore essential. In female fruit flies (*Drosophila melanogaster*), reproductive behavior is strongly influenced by the presence of other flies. While isolated females delay egg laying during the day, with light inhibiting juvenile hormone production, grouped females overcome this inhibition and lay eggs during daylight hours. This presence of others is detected through motion and image-forming vision. Interestingly though, this social modulation of reproduction is not universal: only a subset of *D. melanogaster* populations exhibit this response to social context, indicating a genetic basis for this social influence. Although genomic regions associated with this variation have been mapped, the causal genes and mechanisms underlying differential responsiveness to social context are not known yet. Therefore, this project builds on recent discoveries in the Billeter lab and aims to investigate the genetic basis of population-level variation in social modulation of egg-laying behaviour in *D. melanogaster*.

Objective

The primary objective of this project is understanding of how genetic variation shapes individual sensitivity to social context in a well-defined behavioural and physiological system. It aims to move from mapped genetic associations toward causal understanding of how genetic variation shapes social modulation of reproduction.

R1

The Effects of tACS on Reading Ability

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Background

During reading, eyes make rapid saccades with brief fixations (200-250 ms), processing foveal words while previewing 1-2 parafoveal words to the right, which speeds reading by 20-50 ms per word (Kornrumpf et al., 2017). Research has shown that posterior alpha oscillations (8-13 Hz) lateralization may index spatial attention: ipsilateral power is hypothesized to suppress distractions from unattended hemifields, while contralateral desynchronization may facilitate processing of attended stimuli, potentially producing a natural rightward bias in left-to-right reading (Kornrumpf et al., 2017). To establish alpha's causal role in saccades and reading, alpha-frequency transcranial alternating current stimulation (tACS) over parietal regions could be applied: if it shifts the rightward attention bias, it would alter visuospatial attention during reading.

Objective

This project tests if lateralized occipito-parietal alpha-tACS (10 Hz) causally modulates visuospatial attention, eye movement timing, reading speed, fixation durations, preview benefits, regressions, and word skipping during natural sentence reading. It is hypothesized that left-hemisphere tACS reduces rightward bias and speeds, right-hemisphere enhances them, with saccade onsets phase-locked to stimulation rhythm.

Design/methods

The aim is to recruit thirty-six participants (18 already collected). Participants will be asked to read 180 English sentences taken from Frank et al., (2013) while eye movements are recorded at 1000 Hz (EyeLink 1000). After the trial, comprehension questions will be asked. A 3X2 within-subject design is used, stimulation is either given left/right/or sham tACS, and moving window (no-window/window), the conditions are counterbalanced per sentence. The gaze-contingent window will limit rightward preview to 4 letters; whereas the rest of the sentence will be masked with the letter "x" in parafoveal vision. Latin-squared balanced tACS blocks apply 10 Hz, 1.5 mA peak-to-peak stimulation (~10 min) over O1/O2 and P3/P4 or sham (same stimulation parameters are used, but stimulation will only last 30 s to imitate the sensation of tACS).

Possible implications

Outcomes may provide causal evidence linking alpha lateralization to reading via attention and previewing. If rightward-biased alpha facilitation measurably improves text processing, it could have potential as a neurostimulation intervention for conditions with attentional or reading deficits, such as dyslexia and/or ADHD. If successful, the approach could be adapted as a protocol for speed reading training in consumer neurotech (cognitive enhancement).

R2

Social Exposure and Its Impact on the Onset and Progression of Amyloid-Tau Pathology, Neuroinflammation, and DMN Integrity in Alzheimer's Disease

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Background

It has been shown that decreased social contact is linked to an increased risk of developing Alzheimer's disease (AD), with social dysfunction being a common neuropsychiatric feature across various brain disorders. One of the known neurocircuitries involved in social functioning and affected in neuropsychiatric disorders, is the default mode network (DMN). By investigating how social exposure affects the onset and progression of amyloid-tau pathology and neuroinflammation in AD, as well as connectivity within the DMN, potential new approaches for therapeutic strategies could emerge.

Objective

The project aims to investigate how differences in social group size affect onset and progression of AD pathologies and DMN integrity. In particular, differences in immunohistochemical markers for amyloid- β peptides, hyperphosphorylated tau, neuroinflammation and white matter integrity (DMN) will be examined. It is proposed that enhanced social exposure postpones both onset and progression of AD features, potentially in a sex-dependent manner. This will be put into context to address social contact as a modifiable AD risk factor and present it as a potential preventative intervention strategy.

Design/methods

Male and female 3xTg-AD mice will be placed into either solidarity, pair or group conditions for six weeks. Subsequently, they will be tested for behavioural differences. After transcardial perfusion, brains will be collected and immunohistochemical staining and microscopy will be used to assess differences in pathological markers.

S1

The Role of GPRCR146 on Food Entrainment in Mice

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Background

In mammals, the suprachiasmatic nucleus (SCN) functions as the master circadian pacemaker and is primarily entrained by the light-dark (LD) cycle via retinal input. In addition to photic cues, nonphotic zeitgebers such as time-restricted feeding can phase shift circadian rhythms and drive food-anticipatory activity independently of the SCN. Previous research has shown that peripheral clocks, notably in the liver, are strongly entrained to feeding schedules ¹. G-protein-coupled receptor 146 (GPR146), expressed in the liver and adipose tissue, has recently been investigated for its role in cholesterol and lipoprotein metabolism ².

Objective

Given the strong feeding-driven entrainment of hepatic clocks and the emerging role of GPR146 signalling in energy metabolism, this project will test whether GPR146 functions as a nutritional signal transducer that links nutrient-derived hormonal cues to liver clock function and food-entrainable circadian outputs.

Design/methods

This study will assess the role of GPR146 in behavioural food entrainment by comparing behavioural measures and tissue-level clock gene expression between GPR146 knockout mice and wild-type Per1-luciferase reporter controls. Animals are subjected to time-restricted feeding during the light phase. For the behavioural analysis, food anticipatory behaviour will be scored and compared between experimental groups, followed by the recording of hepatic clock gene expression using a luminometer. Finally, GPR146 distribution in the SCN and other brain regions will be assessed using immunohistochemical staining and/or RNA FISH to localise putative central brain areas through which the receptor may interact with circadian networks.

Conclusion

We hypothesise that GPR146 KO mice show reduced or absent food anticipatory behaviour compared to the wild type. In addition, we hypothesise that tissue cultures of the liver show impaired per1 luciferase rhythms in the KO group but not in the control group. These findings provide novel and valuable mechanistic insights into the role of nutritional cues on our circadian rhythms. These findings may reveal new pathways through which diet, obesity and altered feeding schedules influence circadian organisations and may have broader health implications.

S2

Investigating the Dynamics of Saccadic Attention using Rapid Invisible Frequency Tagging (RIFT)

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Background

Rapid Invisible Frequency Tagging (RIFT) is an emerging technique that uses high-frequency luminance or contrast modulation (typically >60 Hz) to elicit steady-state neural responses without the distracting, visible flicker associated with traditional SSVEP methods, which typically rely on 5-25Hz frequencies. In the past, RIFT required expensive specialized projectors and Magnetoencephalography (MEG). However, recent proof-of-concept evidence showed that RIFT is feasible using a high-speed consumer-grade hardware and Electroencephalography (EEG). This shift toward more accessible hardware facilitates the study of visuospatial attention under more naturalistic conditions, where the almost imperceptible flicker can reduce participant distraction and fatigue.

Objective

The primary objective of this study is to investigate the neural dynamics of saccadic attention. Specifically, the focus is on how the allocation of attention shifts before, during, and after saccadic eye movements. By utilizing RIFT as a continuous attentional tracker, the study aims to map the spatio-temporal dynamics of attentional spotlight during the active gaze shifts while maintaining the invisibility of the flicker, a challenge often complicated by retinal smearing during eye movements.

Design/methods

Participants will view stimuli presented on a consumer-grade 480 Hz OLED monitor. Stimuli will be modulated at RIFT frequencies (e.g., 60 Hz or 64 Hz) and will utilize a wide edge taper to minimize the visibility of the flicker during the rapid retinal displacement caused by saccades. High-speed eye tracking will be integrated to monitor gaze position and precisely time the neural responses relative to saccade onset and offset. Neural activity will be recorded via EEG, and the tagging response will be quantified through cross-coherence analysis between the recorded brain signals and a photodiode capturing the monitor's actual luminance output. Finally, flicker (in)visibility will be formally assessed via a post-experiment questionnaire to validate the efficacy of the edge tapering strategy.

Conclusion

This study aims to demonstrate that RIFT can be effectively used to track attentional allocation during active eye movements without the distracting influence of a visible flicker. The findings could confirm that pairing a high-speed OLED hardware with EEG-based RIFT provides a cost-effective toolkit for exploring the cognitive processes involved in visuospatial attention.

T1

The Role of Theta Oscillations in Memory Retrieval

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Background

Place cells in the hippocampus are known to represent an animal's location in space (O'Keefe & Dostrovsky, 1971). During navigation, theta oscillations organise place cell firing into sequences that reflect past, present, and likely future locations. Stachenfeld et al. (2017) have more recently shown that by encoding future trajectories, place cells support the learning of predictive maps (successor representations [SR]) with respect to rewards. These predictive maps can be learned through biologically plausible plasticity mechanisms (STDP) that rely directly on theta oscillations (George et al., 2023). Complementary *in vivo* studies provide evidence that silencing theta oscillations disrupts memory retrieval in spatial navigation, even though place cells remain intact (Etter et al., 2023). This suggests that while theta oscillations may not be necessary for encoding spatial maps, they may be for retrieving predictive maps and for precisely timed decision-making. Abolishing theta should disrupt such decision-making, while keeping place cells unaffected. The exact mechanisms of how theta oscillations enable the formation and retrieval of predictive maps and affect real-time decision-making in spatial navigation, remain however unclear.

Objective

This project's overall objective is to investigate how theta oscillations govern the formation and retrieval of SR-like predictive maps in reward-guided navigation and decision-making. Specifically, it investigates the necessity of theta oscillations for SR formation and retrieval, and how theta frequency modulation by locomotor speed affects their acquisition and recall.

Design/methods

A spiking neural network model (George et al., 2023) will be used in which CA1 cells learn SR-like predictive maps from upstream CA3 neurons via STDP and theta phase precession. This approach will be complemented by RatInABox (George et al., 2024) to generate place cell activity in RL environments. Agents will perform a reward-guided, memory-dependent delayed non-match-to-place task in a T-maze. Simulations will manipulate theta oscillations during learning and/or retrieval, including intact theta, complete disruption, and theta frequency modulation, depending on the respective objective.

Conclusion

This project has the potential to advance our understanding of how memory is encoded and retrieved in real time. By using a biologically plausible model of hippocampal representations, it could uniquely demonstrate the role of theta oscillations in memory-guided navigation and explain why disrupting theta impairs memory retrieval despite intact spatial representations.

T2

Youth Anxiety CBT Outcomes in a Threat-Processing Framework: IPD Evidence and Severity Score Translation

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Background

Neurobiological models of anxiety implicate heightened activation in networks involving occipital, limbic, and dorsal medial prefrontal regions, supporting threat detection and monitoring. Cognitive behavioral therapy (CBT), has been associated with reductions in anxiety severity and changes in threat-related reactivity in adults. However, despite anxiety disorders being among the most prevalent psychiatric conditions in children and adolescents, evidence regarding treatment effectiveness across specific pediatric anxiety disorders remains comparatively scarce and underpowered.

Objective

The primary aims of this study are (1) to estimate the effectiveness of CBT in youth across anxiety disorder diagnoses using harmonized treatment outcomes, and to examine whether treatment effects differ by diagnosis and baseline severity; and (2) to evaluate the correspondence between widely used pediatric anxiety severity instruments and develop translation models enabling reliable conversion of scores across measures.

Design/methods

The present study will address combined individual participant data from 82 clinical studies (N = 1,028 participants aged <18 years). Using logistic regression and confirmatory factor analysis, this project aims to produce robust, diagnosis-sensitive estimates of CBT outcomes and practical crosswalk functions between assessment tools, facilitating both clinical interpretation and future large-scale research synthesis.

Results

NA

Conclusion

NA

U1

Thermoregulation and Sleep homeostasis during Hibernation Arousals in the Garden Dormouse

Wies van der Hout

Background

Hibernation in mammals consists of long bouts of deep torpor, with strongly reduced metabolism and body temperature. These torpor bouts get interrupted by shorter, energy-demanding arousals to euthermia. The function of these arousals is not completely clear yet. One leading hypothesis is that animals “wake up to sleep”. At very low brain temperatures, normal restorative sleep cannot occur. Sleep pressure is therefore thought to accumulate during torpor and is released during arousals. However, recent work in garden dormice suggests that simply reaching euthermia can reset the torpor–arousal cycle, even when little sleep occurs, highlighting an important role for temperature-dependent metabolic recovery.

Objectives

This project aims to clarify the roles of sleep and body temperature in driving arousals during hibernation.

Design / Methods

Hibernating garden dormice will be externally rewarmed shortly before predicted spontaneous arousals to induce euthermia. Once euthermic, animals will be sleep-deprived for several hours using gentle, continuous stimulation. Nest temperature will be recorded continuously to determine whether animals immediately re-enter torpor, prolong arousals to sleep, or show intermediate responses.

Conclusion

By combining sleep deprivation experiments with thermoregulator measurements, this project will test whether arousals are primarily needed for sleep and/or for temperature-dependent recovery, refining models of hibernation and sleep function.

U2

Combining real and simulated neurons to evaluate predictive hippocampal representations

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Background

Hippocampal place cells represent space through firing in preferred locations (“place fields”) which were long thought to be symmetrical, and so, simulated with Gaussian-based models. However, the shape of place fields becomes increasingly asymmetric with experience navigating through an environment. Thus, the hippocampus could also be encoding a predictive map, which can be implemented through a ‘Successor representation (SR)’ model. But, the SR model still cannot completely match real data observations and the determinants of hippocampal representations under non-rewarded actions remain unknown.

Objective

This project aims to establish the determinants of hippocampal activity by examining real data and modeling it using Gaussian and SR approaches.

Design/Methods

The real data consists of calcium imaging recordings from five B6 mice, which ran on a linear track with either reward at both ends of the track, no reward, or a tone condition in which triggering the tone on one end was necessary to obtain reward on the other end. Thus, Python will be used for analyzing the calcium imaging data, creating the Gaussian and Successor models and performing the statistical analysis. The models will be compared against each other using representational similarity analysis (RSA).

Expected Results

We hypothesize that the predictive (SR) model will be better than the Gaussian model to explain hippocampal activity when there are rewards, and that hippocampal neurons represent a complex combination of not only reward prediction but also its expected location in space (i.e. mental distance to reward) shaped by experience.

Possible Implications

The project aims to establish how the hippocampus learns to predict future actions, which is a core process of cognitive function in our everyday lives. This could be essential not only to further understand how the brain creates cognitive maps, but also to establish how experiences shape these cognitive maps of the outside world.

V1

Alzheimer's Disease Early Detection Using Human EEG Signals

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Background

Alzheimer's Disease (AD) is a common neurodegenerative disorder characterized by progressive cognitive decline. Early-stage detection remains difficult, as clinical symptoms may be subtle despite the already established neuropathological changes. Electroencephalography (EEG) serves as a non-invasive and cost-effective technique that may capture early functional alterations, including slowing in rhythms, decreased coherence between brain regions, and interictal epileptiform discharges. Machine learning has become a useful tool for extracting informative patterns from EEG data. Supervised learning methods using spectral features are able to distinguish AD patients from healthy controls with moderate accuracy, sensitivity and specificity, supporting the use of EEG-based machine-learning approaches in the study of AD.

Objective

The project evaluates whether resting-state EEG signals can be used to distinguish AD patients from healthy controls using machine-learning approaches. It aims to replicate and extend existing EEG-based classification pipelines, and test whether more advanced architectures, such as temporal convolutional networks, will improve the performance metrics (accuracy, sensitivity, or specificity) relative to simpler classifiers used in previous literature.

Methods

An existing dataset of resting-state EEG recordings from AD patients and healthy controls will be used, including Mini-Mental State Examination (MMSE) scores. Data will be processed with the MNE-Python toolbox and spectrograms will be extracted. Using PyTorch, a labeled dataset will be created and a classifier neural network will be trained to discriminate groups. Performance will be assessed using accuracy, sensitivity and specificity.

Conclusion

By replicating and extending the EEG-based classification pipelines, this project will help assess the utility of combining EEG and machine learning for AD detection. The findings could support the development of timely screening strategies, inform early clinical decision-making, and contribute to research on EEG-based biomarkers.

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