ÉCOLE DOCTORALE
Environnements - Santé
Bourgogne | Franche-Comté

30e EDITION

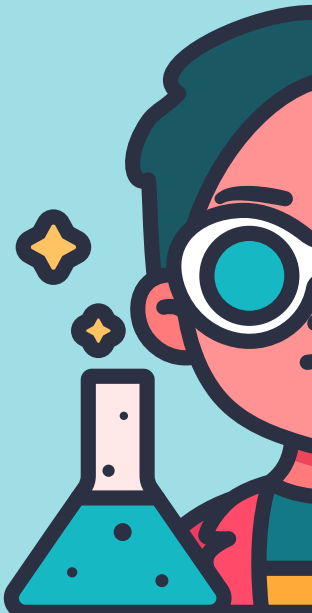
FORUM DES JEUNES CHERCHEURS

DOCTEURS DE DEMAIN

5 juin 2025

SESSION
SANTÉ, ONCOLOGIE ET IMMUNOTHÉRAPIES

13:00 - 15:00



Are community dwelling older adults with impaired functional reserves differ from those who have none transversal study of intrinsic capacities

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Résumé

Background : Projections show that the world's elderly population will continue to grow. This could lead to a number of socio-economic, medical and economic problems associated with a gradual decline in physiological reserves. It is against this background that the World Health Organisation has made healthy ageing a priority for 2015. The aim is to focus on people's ability to be and do what they value. Intrinsic capacities was developed to measure the capacity of individual older adults at a given moment in time. They can be used to detect deviation from healthy aging norms and thus take preventive measures to maintain healthy aging. Over the past five years, intrinsic abilities have been linked to many other factors. However, it is unclear whether they accurately reflect functional ability.
Method : This is a transversal prospective cohort study of a representative sample of community-dwelling people in France. 4 of the 5 domains of intrinsic capacities were assessed. Locomotion (walking speed, chair rise test), vitality (nutritional status, grip strength), cognition (MOCA), psychological (PHQ-9). Other areas of health were assessed. Physical fitness such as physical activity, sedentary time and balance will be assessed using an ActiGraph accelerometer, and the Mini-Best test respectively. Health outcomes will be assessed using PHQ-9. Other covariates such as age and co-morbidities are also assessed.

Results : The preliminary results are based on 58 people (average age 72.2 years) who completed the four domains of intrinsic abilities. 26 were classified in the Functional Impairment group and 32 in the Heath group. A comparison between the groups showed no statistically significant differences for any of the analysed variables: sedentary lifestyle ($p = 0.526$), physical activity ($p = 0.153$), balance ($p = 0.06$) and quality of life ($p = 0.53$).
Conclusion : Our results are not in line with other studies who have analysed the correlation between score in different IC domain and variable like gender, physical activity, walking speed and show correlation between high self-rated health and high IC. This can be explained by our small sample size at this time. One of a big consideration is in both groups sedentary time is considered high according the WHO recommendation which may explain our results under groups analysis may be a valuable approach to explain it and added clinical value to this concept. Specific analysis can help us to better understand this concept and use it in clinical practice.

*Intervenant

Mots-Clés: Intrinsic capacity, elderly, healthy aging, functional performance

Souhait de mort et demandes d'euthanasie et de suicide assisté exprimées par des patients en fin de vie et suivis en Unités de Soins Palliatifs

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Résumé

La fin de vie et plus particulièrement la question de l'euthanasie et du suicide assisté font l'objet de vifs débats éthiques qui touchent à la fois le domaine politique, juridique, sociétal et celui du soin. L'assistance au suicide et l'euthanasie, autorisées dans une quinzaine de pays dans le monde - dont la Belgique, la Suisse, l'Espagne, les Pays-Bas, le Luxembourg ou encore le Portugal et l'Autriche au niveau européen - nécessitent l'intervention d'une tiers personne mais avec un degré d'implication très différent. Dans le contexte français qui n'autorise pas ces deux pratiques qui sont parfois groupées sous le terme " d'aide à mourir ", des patients gravement malades expriment pourtant un *souhait de mort* (Albert and al, 2005) voire une demande d'euthanasie et/ou de suicide assisté (Chassagne, Mathieu-Nicot, Giffard and al, 2025).
Dans ce contexte particulier, l'ambition de ce travail de thèse qui se situe au croisement de la socioanthropologie et de la santé publique, est de documenter le plus finement possible ces situations difficiles à partir d'une méthodologie mixte afin de recenser et caractériser les souhaits de mort exprimés par des patients en fin de vie qui bénéficient d'un accompagnement palliatif (à partir de questionnaires quantitatifs composés de questions fermées et questions ouvertes).

Il s'agira ensuite de rencontrer à l'occasion d'entretien et durant des temps d'immersion à la fois le patient ayant exprimé le souhait de ne plus vivre, mais aussi celles et ceux qui l'accompagnent au quotidien durant la fin de sa vie, notamment les professionnels de santé exerçant en soins palliatifs et les proches du patient afin de comprendre leur expérience personnelle et leur vécu.
Enfin, il s'agira de suivre l'évolution des souhaits de mort le plus longtemps possible de façon à déterminer si ces derniers se maintiennent dans le temps et/ou s'ils pouvaient évoluer vers d'autres projets (souhait de limiter ou d'arrêter les traitements, souhait qu'une sédation profonde et continue maintenue jusqu'au décès soit mise en place, souhait de recevoir une euthanasie ou un suicide assisté, idéation suicidaire). Il s'agira également d'identifier si la prise en charge palliative et la gestion des symptômes et des souffrances physiques, psychologiques et sociales peuvent modifier voire faire disparaitre les souhaits de mort.

Mots-Clés: Soins Palliatifs, Souhait de mort, Euthanasie, Suicide Assisté, Ethique de la relation, Etude qualitative

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Préparation des acteurs d'une maison de santé en France à l'approche " Goal-oriented care " : étude pilote

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Résumé

Introduction

La multimorbidité, définie comme la coexistence d'au moins deux maladies chroniques chez une même personne, constitue un défi croissant pour les systèmes de santé. Elle entraîne des répercussions multiples, tant pour les personnes concernées que pour leurs proches et les professionnels de santé. Fréquemment associée à d'autres facteurs de vulnérabilité, elle complexifie considérablement les parcours de soins.
Pourtant, l'approche encore dominante, centrée sur les problèmes et fondée sur des recommandations élaborées maladie par maladie, ne permet pas de répondre de manière adéquate à cette complexité. La multiplicité des intervenants favorise la fragmentation des soins et alourdit la charge de traitement. Par ailleurs, un décalage peut exister entre les objectifs médicaux poursuivis et les priorités personnelles des patients.

Dans ce contexte, le modèle des *Goal-oriented care* (GOC), ou de l'aide et des soins centrés sur les objectifs de la personne (ASCOP), propose un changement de paradigme. Plutôt que de se focaliser uniquement sur les problèmes, il s'agit de coconstruire avec le patient un plan de soins aligné sur ses objectifs. Cette approche repose sur un processus itératif et dynamique, impliquant activement les patients et leurs proches et prenant en compte leurs valeurs, préférences et contexte de vie.

De plus en plus reconnue à l'échelle internationale, notamment dans les soins primaires, cette approche nécessite une préparation préalable des professionnels et des patients afin d'en faciliter l'appropriation et la mise en œuvre.

Méthode

Cette étude pilote, menée au sein d'une maison de santé pluriprofessionnelle en France, s'inscrit dans une démarche de recherche-action participative. Elle vise à documenter et analyser le processus de préparation à la mise en œuvre de l'approche *Goal-Oriented Care* (GOC), à partir des expériences croisées des patients et des professionnels.
Le protocole prévoit notamment une formation conjointe à cette approche. Une méthodologie mixte est mobilisée pour évaluer l'évolution des connaissances et compétences, l'acceptabilité du modèle, ainsi que l'expérience du partenariat en santé telle que vécue par les participants.
Les cadres théoriques, les méthodes de recherche retenues et les perspectives de l'étude sont également présentés.

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Mots-Clés: Multimorbidité, Goal, oriented care, Recherche action

Study of the cleavage state of N-cadherin on the surface of high-grade bladder cancer cell small extracellular vesicles

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Résumé

Background and purpose: Small Extracellular Vesicles (sEVs) are produced and secreted by cancer cells. They carry bioactive molecules (proteins, lipids, RNA, DNA) and transfer them into recipient cells, thus modifying their functions. N-cadherin was identified as a progression marker of high-grade urothelial carcinomas involved in cell motility, proliferation, cell invasion and angiogenesis. It is cleaved by the ADAM10/Tspan15 complex at the plasma membrane to produce an extracellular fragment NTF and a CTF-1 fragment anchored to the plasma membrane. CTF-1 is then cleaved by the γ-secretase complex, releasing a CTF-2 fragment that activates proliferative genes. We previously found the entire N-cadherin and the CTF-1 fragment in sEVs produced by high-grade T24 bladder cancer cells. In this work, the presence of ADAM10 and Tspan15 was analyzed on sEV membrane to determine the possibility of N-cadherin cleavage. The impact of T24 sEVs on low-grade RT4 bladder cancer cells was investigated to analyze whether these vesicles could modify their proliferation.

Material and Methods: sEVs were isolated by differential ultracentrifugation of T24 cell supernatants and characterized by NTA (size and concentration), MET (morphology), and western blotting (presence of sEV markers). N-cadherin, ADAM10, and Tspan15 expression was assessed by immunoblotting at the cell membrane and in sEVs. T24 sEV interaction with low-grade RT4 bladder cancer cells (N-cadherin negative) was monitored by confocal microscopy, and RT4 cell proliferation was analyzed using the Incucyte instrument.

Results: Following T24 sEV complete characterization, this study confirmed the localization of entire N-cadherin and CTF-1 fragment at the vesicle membrane as well as active ADAM10 but not Tspan15. Furthermore, RT4 cells did not internalize T24 sEVs but an increase in RT4 cell proliferation was observed when they were treated with T24 sEVs.

Conclusion: The presence of CTF-1 at the vesicular level was not the result of the ADAM10/Tspan15 mediated-cleavage of N-cadherin since there was no Tspan15 at the vesicle membrane. T24 sEVs would act on RT4 cells through cell surface receptors to increase their proliferation. The absence of vesicular Tspan15 would allow the entire N-cadherin to be maintained on vesicles. N-cadherin expressing sEVs remain on the surface of RT4 cells and possible interaction of vesicular N-cadherin with RT4 cell surface receptors could increase their proliferation and promote tumour progression. SEVs, isolated from the urine of bladder cancer patients, and expressing entire N-cadherin on their surface, could be used as prognostic marker of

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disease progression.

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Jason BERNAUER

Mots-Clés: small extracellular vesicle, N, cadherin, ADAM10, tetraspanin 15

Role of NRLP3 in CD8 T cell biology

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Résumé

Immunotherapy using immune checkpoint inhibitors (ICIs) has recently emerged as a promising therapeutic option for many cancers. However, response rates rarely exceed 40%, notably due to the inability of CD8 T lymphocytes to infiltrate the tumor site. The NLRP3 protein is a member of the Nod-like receptor family, and its role has been particularly well described in myeloid cells, where it can form the NLRP3 inflammasome, involved in the maturation of pro-inflammatory cytokines such as IL-1β. In lymphoid cells, our team has observed that NLRP3 is induced via an IL-2/STAT5-dependent pathway during T cell activation. It plays an inflammasome-independent role as a transcription factor in Th2 lymphocytes (Bruchard et al., 2015). In Th17 lymphocytes, NLRP3 is involved in the TGFβ pathway, leading to an increase in their immunosuppressive functions (Accogli et al., 2025). However, data regarding its function in CD8 T cells remain scarce.
We have shown that the IL-2/STAT5 pathway regulates NLRP3 expression in CD8 T cells. In CD8cre x NLRP3flox mice that we generated, we observed slower tumor growth in certain tumor models. Three key observations are associated with this delay. First, we noted an increased infiltration of CD8 T cells into the tumors, which was not due to enhanced proliferation, but rather to CXCR3 overexpression. In addition, CD8cre NLRP3flox cells displayed increased cytokine production and reduced exhaustion. At the molecular level, it appears that a TCR–IRF4–Tbx21 axis-dependent pathway is modulated by NLRP3, leading to these phenotypic changes.
In conclusion, our study highlights the essential role of NLRP3 in regulating CD8 T cell biology, particularly in the tumor context. These findings open new perspectives for enhancing the efficacy of immunotherapy, especially by targeting NLRP3 regulation in CD8 T cells to boost their anti-tumor response.

Mots-Clés: NLRP3, CD8 T cell, Cancer

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Resident memory T cell analyses revealed a CXCR6-PD1+ subpopulation with increased stemness features in patients with metastatic colorectal cancer

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Résumé

Tissue resident memory (TRM) T cells have emerged as key players in cancer immunosurveillance, and their presence has been linked to a favorable clinical outcome in solid cancer patients. Liver metastases exhibit a highly immunosuppressive tumor microenvironment, however the role and clinical impact of TRM cells infiltration in colorectal cancer remain elusive.
An exhaustive profiling was conducted on tumor infiltrating lymphocytes isolated from 27 patients' colorectal cancer (CRC) liver metastases, and prognostic value of TRM cells was assessed. Cytokine production, as well as exhaustion phenotype and proliferation capacities were evaluated in *in vitro* differentiated TRM cells. Further analyses included cytotoxic assessment in 3D spheroids models, scRNA sequencing analyses and protein expression kinetics upon activation. The aim was to understand TRM subpopulation differences and relationship.

Our analyses highlighted two important and distinct TRM subpopulation based on CXCR6 and PD1 expression, which were predictive of recurrence free survival (RFS). Interestingly, we found that the bad prognosis associated subpopulation (CXCR6+PD1-) secreted less IL2, TNFα and expressed less CD107a upon activation. The use of a CXCR6 inhibitor in 3D spheroid models also showed increase in CD107a expression and reduced spheroid size, suggesting that CXCR6 expressing TRM cells are indeed less efficient. This observation was further enforced by scRNA sequencing and flow cytometry analyses, which linked a terminally exhausted phenotype (TCF1-TOX+BACH2-) to this population and a progenitor exhausted phenotype (TCF1+TOX-BACH2+) to the good-prognosis associated subpopulation (CXCR6-PD1+). The expression of other inhibitor associated molecules, such as CD39, TIGIT and LAG3 sharped this exhausted phenotype. CXCR6+PD1- TRM cells also showed limited Ki67 expression in a kinetic model, and acquired exhausted associated features faster compared to CXCR6-PD1+ TRM cells.

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We identified a novel population of TRM cells CXCR6+PD1- that exhibit a 'stem-like' phenotype, with better efficiency, higher proliferation capacity and associated with improved prognosis in metastatic CRC patients.

Mots-Clés: Lymphocyte T résident mémoire, Cancer colorectal, Immunothérapie

Evaluation du dasatinib et du ponatinib pour le contrôle de la fonctionnalité de CAR T cell ciblant CD123

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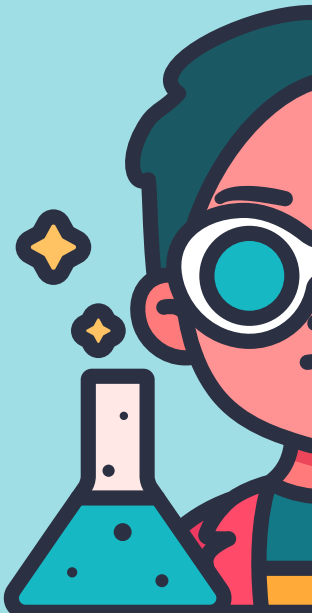

Identification of the molecular bases of malformation syndromes with or without intellectual disability using omics data

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Résumé

The thesis project is part of a European initiative aimed at identifying the causes of rare diseases in patients who have not yet received a molecular diagnosis.
The first part focuses on the Solve-RD project (Solve Rare Diseases), a European research initiative under the Horizon 2020 program of the European Commission. The objective is to solve a significant number of rare diseases whose molecular causes remain unknown by using innovative approaches that combine integrated multi-omic technologies.
The work will involve the interpretation of already generated multi-omic sequencing data (short-read and long-read genome, deep exome, RNA-seq, and epigenome) from tissues of individuals affected by Pai syndrome and oculo-auriculo-fronto-nasal syndrome (OAFNS).

These conditions, despite being extensively studied for years, still do not have identified causes. In response to this, our approach proposes new strategies that integrate multi-omic data to explore potential pathophysiological mechanisms. Several hypotheses for pathophysiological mechanisms are put forward:

-A hypothesis of a constitutional monogenic disease, due to variations that are not detectable by exome or short-read genome sequencing, such as non-coding intronic variations, regulatory regions, intergenic regions, and structural rearrangements. To detect these variations or genes of interest, several types of analyses will be conducted: long-read genome sequencing (lrGS), transcriptome, proteome, and epigenome.
-A hypothesis of somatic mosaic disease, due to variations that are undetectable in the blood. A study of the affected tissue using deep exome sequencing will be conducted and compared with healthy tissue to highlight these variations.
-A hypothesis of oligogenic disease, due to variations affecting at least two genes within the same molecular pathway.

*Intervenant

These hypotheses will broaden diagnostic perspectives by exploring molecular leads.

The second part of the thesis work will focus on the ERDERA project (The European Rare Diseases Research Alliance), which, like the Solve-RD project, aims to reduce the diagnostic deadlock.
ERDERA aims to have a major impact on rare diseases by supporting patient-centered research to improve diagnostic pathways, develop new treatments and harnessing the potential of health and research data.
As part of this project, exome, genome, and omics data from patients experiencing a diagnostic odyssey will be shared for reanalysis and reinterpretation using various tools, updated databases, recent advances from literature and clinical practice, as well as new analysis strategies. The thesis work will involve reinterpreting the data to establish a diagnosis.

Mots-Clés: Rare diseases, Omics data, Reanalysis, Molecular bases, Diagnosis odyssey, Bioinformatics

One-pot Hantzsch/click for synthesis of new MTDLs compounds with cholinesterases, antioxidant and calcium channel inhibition properties

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Résumé

Introduction: This work focuses on multitarget-directed ligands (**MTDLs**) as strategy for Alzheimer's disease (**AD**) treatment. AD has a complex mechanism involving many pathophysiological processes including amyloid plaques, neurofibrillary tangles, oxidative stress, calcium dyshomeostasis and neuronal loss leading to a cholinergic deficit. There is therefore an urgent need to develop **disease-modifying drugs** influence the pathophysiological processes. The original approach of this work is the association of Hantzsch multicomponent and click reaction in one-pot condition to synthesize these new MTDLs. This process aligns with **green chemistry** principles by reducing waste and derivatives formation.
Results: We designed hybrids molecules containing dihydropyridine moiety as calcium channel antagonist, with tacrine as cholinesterase inhibitor. The biological evaluation revelated significant anticholinesterase, antioxidant, neuroprotective, and calcium channel inhibitory

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activities. Among the synthetised compounds, **IIIj** exhibited a promising multitarget profile and demonstrated antiamnesic efficacy in scopolamine-induced amnesia mouse model, confirming its potential for AD treatment.
Conclusion: By combining the properties of dihydropyridine and tacrine, we have developed 18 multi-targeted compounds demonstrating inhibition of enzymes involved in disease progression, antioxidant capacity as well as calcium inhibition. The result from evaluation shows that compound **IIIj** could hold interesting properties for being therapeutic candidate for AD. This work validates the potential of MTDL strategy, and our process of one-pot tandem synthesis is a significant advancement in medicinal chemistry.

Mots-Clés: Keywords: Alzheimer's disease, disease, modifying drugs, multitarget directed ligands, one, pot, green chemistry, multicomponent reaction.

Targeting of inflamed intestinal regions using fluorescent siRNA-based microparticles in a colitis murine model

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Résumé

Inflammatory Bowel Disease (IBD) represents a group of conditions affecting millions of people. Our team has developed a patented gastro-resistant nano-in-micro formulation for oral delivery. The lipid nanoparticles (LNPs) encapsulate anti-TNFα siRNA, which has demonstrated therapeutic efficacy.
The objective of this study was to evaluate the targeting efficiency of inflamed intestinal regions using dual fluorescent labeling in a TNBS-induced colitis murine model. To achieve this, we successfully labeled the LNPs and microparticles with distinct fluorophores. Polyethylene glycol (PEG), one of the four components of the LNPs, was conjugated to Cyanine 5 prior to formulation. Microparticles were conjugated with fluorescein before encapsulating the LNPs. This wavelength difference enabled us to perform simultaneous biodistribution studies.

For the LNPs, different PEG-Cy5 ratios (10%, 25%, 75%, 100%) were tested. We evaluated particle size and polydispersity index (PDI). Higher PEG-Cy5 content resulted in increased nanoparticle size, so the 10% formulation was selected for its similarity to the control. Microparticles were optimized at 1%, 2.5%, and 5% polymer-FLU ratios. The 5% formulation yielded particles under 200 μm (size: 136 μm), which met our criteria.

In vivo studies were conducted with two groups of mice (n = 7): one healthy, one colitis-induced. After three days of oral administration, mice were sacrificed, and intestinal tissues

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were collected, lyophilized, and extracted in ethanol to measure fluorescein fluorescence. Results revealed increased accumulation in the proximal colon of inflamed mice. The selective release of microparticles in these regions is attributed to their mucoadhesive properties and aligns with the TNBS inflammation profile.

Confocal microscopy on transverse colon sections from one mouse per group confirmed colocalization of nanoparticles and microparticles in inflamed tissues. No fluorescence was observed in healthy mice, emphasizing the specificity of our system.

In this work, we successfully developed a dual fluorescent labeling strategy, allowing for the independent tracking of both LNPs and microparticles. This enabled us to monitor the behavior of each component throughout the formulation and delivery process. Our results demonstrated a preferential accumulation of the system in inflamed intestinal areas, confirming the targeting potential. Furthermore, the study validated the feasibility of using orally administered microparticles to transport siRNA-loaded nanoparticles specifically to sites of inflammation.
Future work will focus on investigating the in vivo release kinetics of LNPs from microparticles to better understand the dynamics of siRNA delivery. We plan to assess the potential for systemic absorption that we expect low

Mots-Clés: Fluorescence, Nanoparticules, In vivo

Clinical relevance of the reverse lipopolysaccharide transport pathway in patients with acute peritonitis and mechanistic insights from a murine model

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Résumé

Aim and background: Sepsis is a life-threatening condition characterized by organ dysfunction due to a dysregulated host response to infection. The Reverse LPS Transport pathway (RLT), involving the Phospholipid Transfer Protein (PLTP) and high-density lipoproteins (HDL), was shown to play a crucial role in neutralizing and eliminating bacterial lipopolysaccharides (LPS) in animal studies. However, there is a lack of clinical evidence of this pathway in humans.
Methods: The LIPS study involved 27 patients with peritonitis and endotoxemia. Plasma samples were collected at different time points. Peritoneal fluids were collected during surgery. Lipoprotein profiles, LPS concentration and activity, PLTP activity and cytokine concentration were determined. Besides, we followed the distribution of fluorescent Cy5-HDL over 24 hours in mice injected intraperitoneally with LPS (n=5) or saline (n=9).

*Intervenant

Results: In patients with peritonitis, HDLc and PLTP activity were associated with increased LPS clearance at 4 hours post-surgery (-3% (-26;10) vs 29% (13;52), $p< 0.01$ and -2% (-15;10) vs 20% (8:52), $p = 0.03$, respectively). HDL concentration was associated with reduced LPS activity at 4 and 24 hours. HDLc were negatively associated with mortality (2 (14.3%) vs 7 (53.8%), $p = 0.046$). A strong correlation between HDLc as well as HDL-associated LPS in peritoneal fluid and plasma HDLc could be observed ($r = 0.67$, $p < 0.01$ and $r = 0.53$, $p < 0.05$ respectively). We reported a significant increase in Cy-5-HDL in peritoneal fluid of mice injected with LPS compared with control animals (0,312 (0.283;0.390) vs 0,231 (0.132;0.319), $p < 0.05$).
Conclusion: This work provides new insights into the positive effect of HDL and PLTP on LPS clearance in humans. Our findings in humans and mice support that circulating HDL might cross the peritoneum during acute peritonitis with a possible early effect directly at the site of infection to quickly bind LPS.

Mots-Clés: endotoxin, lipoprotein, inflammation, phospholipid transfer protein

EXTRACELLULAR VESICLES TRANSPORT HSP90 TO EXACERBATE PULMONARY FIBROSIS.

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Résumé

Background and aims: Idiopathic pulmonary fibrosis (IPF) is a progressive lung disease involving aberrant intercellular communication. Extracellular vesicles (EVs) accumulate during IPF and carry active biomolecules including Heat Shock Proteins (HSP) which have extracellular roles. We explored whether HSPs are linked to EVs and how this contributes to pulmonary fibrosis progression.

Methods: EVs were isolated from broncho-alveolar lavage fluid (BALF) collected from mice with bleomycin-induced pulmonary fibrosis and from cell culture media by ultracentrifugation. Their functional properties were tested on ex vivo lung tissue followed by transcriptomic and microscopic analyses. The cellular distribution of EVs in fibrotic lungs was studied by flow cytometry. Extracellular HSP90 was monitored by in vivo SPECT-CT imaging.

Results: HSP90 was increased at the surface of BALF-EVs from mice with pulmonary fibrosis compared to control vesicles and was undetected in non-vesicular fraction (western blot). Among lung cell types, these EVs were mainly secreted by fibroblasts and taken up by macrophages (55%+/-6.3%, n=6). Using ex vivo cultured lung tissue, we observed that Hsp90-/-fibroblast-EVs or BALF-EVs incubated with HSP90 blocking antibody had decreased pro-fibrotic properties compared to controls, as observed for the expression of Fn1 ($p=0.03$) and Col1a1 ($p< 0.01$) and second harmonic generation (2-fold decrease, $p< 0.001$). By SPECT-CT analysis, we observed increased extracellular HSP90 in the lung of mice exposed to bleomycin compared to control.

Conclusions: During lung fibrosis, EVs accumulate and transport HSP90 at their surface. HSP90+ vesicles seem to mediate fibroblasts to macrophages pro-fibrotic crosstalk. The inhibition of HSP90 decreases pro-fibrotic EV functions.

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Mots-Clés: Heat Shock Proteins, Pulmonary fibrosis, Extracellular vesicles

The GIP/GLP-1 receptor agonist Tirzepatide improves and regulates hepatic lipid metabolism and glycemic control in obese/diabetic mice

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Satiating and hedonic effects of fat-taste enhancers: a novel tool for obesity treatment - Preclinical studies

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Obesity leads not only to metabolic disturbances, but also to neuropsychiatric disorders, and is therefore associated with emotional and cognitive symptomatology. Its complex and multifactorial aetiology is often exacerbated by emotional overeating, though the neurobiological mechanisms at the origin of excessive feeding are not fully understood. Highly caloric regimens, and in particular fatty diets, impact the immune system and induce systemic and central inflammation and neuroinflammation in the central nervous system, triggering metabolic changes. Particularly, lingual receptor CD36, crucial for oro-gustatory fatty acid perception and involved in hedonic modulation, is downregulated by sustained fat consumption. Obesity therefore changes mechanistic and functional aspects of the reward system, notably in its hypothalamic elements, directly or indirectly affecting food intake regulation. Changes in the permeability of the blood brain barrier (BBB) have been further reported in the hypothalamus, which may affect the anorexigenic activity of local pro-opiomelanocortin (POMC)-expressing neurons, compromising individuals' homeostatic needs. While distinct pharmacological treatments target metabolic aspects of obesity, most neglect its neurobehavioral consequences. We hypothesize that obesity-induced behavioural changes leading to maladapted feeding may be explained by chronic neuroinflammation, and/or result from altered BBB permeability potentially affecting homeostatic and hedonic neuronal processing. In an innovative approach, my doctoral research addresses these scientific questions through the use of the non-caloric fat-taste enhancer NKS-3, a high-affinity CD36 agonist, aiming at *in vivo* modulating fat-taste perception. We use C57BL/6 mice fed a high-fat (HFD) diet as a preclinical model of obesity. The animals are subsequently treated with a 50 µM solution of NKS-3 for 5 to 15 weeks. Following the treatment, various aspects of their behaviour are assessed using a comprehensive battery of behavioural tests. Central inflammation, BBB permeability, reward system and hypothalamic neural network activation are finally evaluated by histological and biomolecular *post-mortem* approaches. Our first results have demonstrated that, while HFD—induced neuroinflammation was reversed by NKS-3, the behavioural disturbances associated with the obese phenotype were not attenuated after 5 weeks of treatment. Ongoing experiments targeting neuro-glio-vascular interactions will certainly give us insight into whether BBB modifications affect neuronal activity in hypothalamic and extra-hypothalamic networks in the context of obesity, and will potentially identify new therapeutic aspects of NKS-3. This study paves the way for future research on feeding behaviour, serving to the development of more effective treatments.

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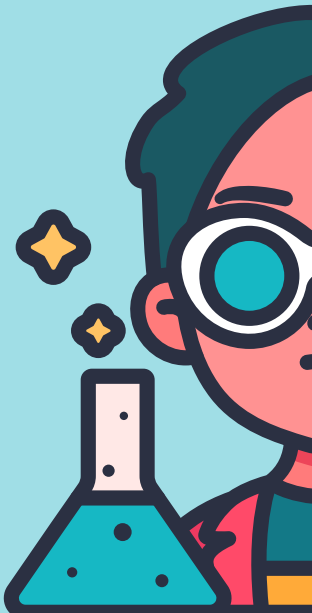

Influence de la réalité virtuelle sur le schéma corporel et l'espace péripersonnel Influence of virtual reality on body schema and peripersonal space

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Résumé

Prism adaptation is a common paradigm used to induce a sensorimotor discrepancy. When subjects wear glasses that shift the visual field during visuomanual pointing tasks, the hand is seen to be shifted from its actual position. When the glasses are removed after adaptation, we can observe sensorimotor aftereffects, i.e pointing errors in the opposite direction of the adapted optical deviation. Furthermore, cognitive aftereffects are also described in space representation. This type of experiment reflects a strong link between sensorimotor plasticity and space representation.
Virtual reality (VR) brings to this research field novelpossibilities for investigating the asymmetrical visuo-spatial manipulations and the consecutive disturbance of sensorimotor coordination. For example, we can easily change the positional gain in specific areas of the space.

In this study, we investigated the changes in peripersonal space (PPS) after sensorimotor adaptation induced by non-homogeneous visuo-spatial perturbations. For this purpose, we developed a new paradigm to generate an heterogenous spatial incorporation using a VR head-mounted display, in right-handed healthy subjects. Here, the visual feedback of a movement was amplified by a factor 3 in the left hemispace, whereas it was divided by a factor 3 in the right hemispace: a 30 cm pointing resulted in a 90 cm visual feedback on the left, and in a 10 cm on the right. Such a manipulation of the sensory motor gain aimed to increase the subject's capabilities in one hemispace, while restricting them in the other one.

To evaluate the effects of the gain changes, we compared subject's sensorimotor performance during two experimental conditions tested before and after the visuo-spatial manipulation session:

- An evaluation of the PPS by assessing the participant's perceived delimitation of his reaching space in the left and right hemispaces

- An estimation of the level of adaptation using an open loop (no visual feedback) pointing task

We predicted the sensorimotor adaptation to be consistent with the applied perturbation.

*Intervenant

Accordingly, we observed that the subjects showed significant sensorimotor aftereffects: 1) In open loop pointing task, a significant hypermetric hand pointing in the right hemispace and 2) a reduction of the PPS associated with the hypermetric movement.
In summary, we induced peripersonal space plasticity in a specific hemispace, consistent with a sensorimotor adaptation following an heterogenous visuo-spatial perturbation. Further investigations are ongoing to determine which factor -side-effect or gain effect- is causing adaptations in a single hemispace.

Mots-Clés: Plasticité sensorimotrice, réalité virtuelle, représentation spatiale

The effect of superimposed local vibration on the time before exhaustion at low and moderate intensity.

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INTRODUCTION: Muscle spindle stimulation with superimposed local vibration (SLV) has shown transient facilitation motor unit recruitment facilitation and increased strength during submaximal contraction (1). Conversely, repeated spindle activation during voluntary contractions reduces support to the α-motoneurons, leading to fatigue and strength loss (2). Thus, applying SLV during fatiguing submaximal contractions delay the decline in strength (known as "performance fatigability"). This study tested the effect of SLV on men and women an intermittent, fatiguing knee extension task at low and moderate intensity of contraction.

METHOD: A total of 45 participants performed maximal voluntary contraction (MVIC) of the knee extensors and flexors before (PRE) and after (POST), a fatiguing task. The fatiguing protocol consisted of intermittent knee extensions (15s effort, 5s rest) at 50% (15 males and 9 females) or 30% MVIC (13 males and 8 females) until a 10% strength target loss. Participants performed the control task (CON) or the vibration condition (SLV) in random order. Vibration was applied to the quadricipital tendon (100 Hz, 2-3 mm). An ANOVA between *Condition* was used for the time to exhaustion (TTE), including statistical parameters *Sex* and *Intensity* (30% vs. 50%) as between-subject factors and *Condition* (CON vs. SLV) as a within-subject factor.

RESULTS: The MVIC decreased from PRE (240 ± 71 N·m) to POST (164 ± 54 N·m) similarly in both *Condition* ($p = 0.834$), *Intensity* ($p = 0.948$) or *Sex* ($p = 0.147$).
The ANOVA revealed a longer TTE at 30% (274 ± 119s) than at 50% (112 ± 28s, $p < 0.001$), and *Sex* did not influence the TTE ($p = 0.245$). The analysis showed that SLV increased by 11 ± 21% the TTE (CON: 179 ± 110s, SLV: 196 ± 121s, $p = 0.007$) without differences between *Intensity* ($p = 0.064$) or S*ex* ($p = 0.120$). No correlation was found between the MVIC and the *Condition* ($p = 0.815$).

CONCLUSION: We found that superimposed local vibration is an efficient method to increase the time before exhaustion at low or moderate intensity in both men and women without altering the force loss after the fatiguing task. Moreover, its positive effect remains consistent regardless of maximal force, suggesting that SLV's influence is independent of individual strength levels. This raises the question of how the chronic use of SLV during resistance strength training may affect performance.

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Comparison of Static Stretching and Nerve Gliding at Varying Intensities: Acute effect of Flexibility, Neural and Muscular Stiffness, and Strength.

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Résumé

INTRODUCTION:

Stretching is an integral part of the sports landscape. However, the mechanisms and structures involved in stretch tolerance remain poorly understood (1). While muscle structures play a key role, other factors are also implicated such as fascia and nervous tissue (2). This study investigated stretching modalities targeting specific anatomical structures (nerves or muscles) at different intensities (at pain threshold and 10% below). The objective is to determine whether nerve-targeted stretching can contribute to reducing muscular and/or neural stiffness and to increasing the range of motion without affecting force production.

METHODS:

21 physically active volunteers (12 women and 9 men) participated in this randomized crossover study. Experimental sessions involved stretching exercises in five conditions: static stretching, nerve gliding flossing performed both at pain threshold and 10% below, and a control condition where participants rested passively.The static stretching protocol included five 60-seconds sets, while nerve gliding was comprised of five 30-repetitions sets at 0.5 Hz combining dorsiflexion/plantar flexion and cervical spine flexion/extension. Testing included maximal voluntary isometric contractions of the right hamstrings, EMG measurements of biceps femoris (BF) and semitendinosus (ST), passive knee extension (PKE), Stand and Reach test (SR), and ultrasound elastography to measure shear wave velocity of the right sciatic nerve and BF. A two-factor ANOVA was used to compare effects before and after the interventions.

RESULTS:

*Intervenant

No significant interaction between condition and time was observed for maximal torque ($p= 0.971$) or EMG activity of the BF ($p = 0.381$) and ST ($p = 0.553$). The control condition had no significant effect on amplitude, whereas all stretching modalities demonstrated a time-dependent improvement. For both PKE and SR, the amplitude increased immediately after the experimental session ($p < 0.001$). Shear wave elastography of the BF muscle significantly decreased after stretching ($p= 0.003$), with no significant differences between conditions ($p= 0.433$). However, the sciatic nerve shear wave elastography decreased over time only in the nerve gliding at pain threshold condition ($p < 0.001$).

CONCLUSION:

All stretching modalities increased the amplitude without significantly affecting strength. However, nerve gliding induced an additional performance gain by reducing shear wave elastography on the nerve, suggesting that stretch tolerance may be partly modulated by nerve properties. Therefore, nerve gliding could be as critical as muscle stretching in optimizing both amplitude and strength, making it an important part of sports training protocols.

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Mots-Clés: Shear wave elastography, Neurodynamic, Range of motion, Hamstring, Sciatic nerve

Influence of the knee and hip joint angles on the knee extensor muscles and tendon shear wave velocity in men and prepubertal boys

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Résumé

Introduction :
The aim of the study was to compare the influence of the knee and hip joint angles on the myo-tendinous elastic properties assessed with shear wave elastography between men and prepubertal boys.

Material and methods :

Twenty volunteers participated in this study including 10 prepubertal boys (10.1 ± 0.9 years old) and 10 men (21.0 ± 1.5 years old). They came to the laboratory for one experimental session that included shear wave velocity (SWV) measurements at rest for the vastus lateralis (VL), rectus femoris (RF), and patellar tendon (PT). These measurements were repeated in 10 randomized positions, incorporating five knee joint angles (30, 50, 70, 90, and 110○) and two hip joint angles (0○: lying and 80○: seated). The collected SWV were analyzed with a three-way analysis of variance, considering the factors of knee angle, hip angle, and age (prepubertal boys vs. men).

Results :

The SWV increased as the knee joint angles increased for VL, RF, and PT. Additionally, RF exhibited greater SWV values at 0○ hip angle compared to 80○ (Mean difference: -0.187). No significant difference was observed between boys and men for VL and RF. However, significantly lower SWV values were observed for PT in boys than in men from 30○ to 90○ knee joint angles ($p < 0.001$).

Conclusion :
The results of the present study suggest that a similar knee and hip joints configuration could be used to assess the knee extensors' myo-tendinous elastic properties in men and prepubertal boys. Additionally, the hip joint angle displayed a large influence on RF SWV, indicating the need to consider hip configuration during inter-study comparisons.

Mots-Clés: Stiffness, Elastography, Children, Quadriceps

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Effects of Contraction Intensity and Ramp Rate on Motor Unit Decomposition and Persistent Inward Currents in Tibialis anterior

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Résumé

Introduction: Identifying action potentials belonging to individual motor units (MUs) provides information about the motor output from the spinal cord. High-density surface electromyography (HDsEMG) offers a non-invasive technique for assessing MUs activity. However, MU identification from the raw EMG signal remains sensitive to contraction parameters such as contraction intensity and force fluctuation (Hassan et al., 2020). These contraction parameters also influence the estimation of persistent inward currents (PICs), a neuromodulation that enhances motoneuron excitability, resulting in higher and more sustained force production (Lee & Heckman, 1998). In humans, PICs are estimated via paired motor unit analysis, where ΔF reflects recruitment–derecruitment hysteresis during triangular ramps (Gorassini et al., 1998). This study aimed to determine the optimal combination of contraction intensity and ramp slope to 1) maximize MU identification, and 2) assess their influence on MUs' behavior and ΔF estimation during triangular isometric ankle dorsiflexion. Methods: Thirty-two healthy participants (19 males, 13 females) completed two experimental sessions separated by two to ten days. HDsEMG signals were recorded from the tibialis anterior using two 64-channel grids. After a familiarization session, participants performed maximal voluntary contractions (MVCs) followed by triangular isometric ramp contractions at different force levels (20%, 30%, 50%, and 70% MVC) and ramp slopes (2%, 3%, 5%, 7%, and 10% MVC.s-1). The number of identified MUs and ΔF were analyzed. Results: For a given contraction intensity, slower ramps (2%-3% MVC.s-1) allowed us to identify more MUs than faster ramps (5–10% MVC.s-1) (all $p < 0.01$). At 2% and 3% MVC.s-1, more MU were identified at 20% than 50% and 70% MVC, respectively (all $p < 0.035$). ΔF was also significantly influenced by ramp rate at 20%, 30%, and 70% MVC ($p \leq 0.005$). Specifically, we observed higher ΔF values at slower ramp rates. Discussion: Slow ramps (2–3% MVC.s-1) allow to identify a higher number of MUs than faster ramps (5–10% MVC.s-1) for a given intensity, likely by reducing temporal overlap and improving spike decomposition. However, within the tested intensities (20%, 30%, 50%, and 70% MVC), MU number declined at

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higher force levels, even at slow ramp slopes, likely due to increased signal complexity that impairs decomposition. The lower ΔF at higher ramp slopes may suggest PICs are not fully activated during fast ramps. Conclusion and Perspectives: Ramp slopes of 2–3% MVC.s-1 optimized MU identification but provided distinct MU characteristics such as ΔF compared to faster ramp slopes.

Mots-Clés: Motor units, Persistent Inward Currents (PICs), High, Density Surface Electromyography (HDsEMG)

Effet aigu des vibrations locales du tendon quadricipital au repos sur la force musculaire du quadriceps et la vitesse de marche maximale chez la personne âgée en EHPAD.

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Résumé

En EHPAD il est fréquent que les résidents soient sujets à un manque de stimulation, des pathologies, une fatigabilité accrue, des douleurs, de l'anxiété, de la dépression, ou encore de la sédentarité. Malgré les recommandations en faveur de l'activité physique chez les personnes âgées institutionnalisées, la pratique physique n'est plus toujours possible ou acceptée. La VL (vibration locale) permet une stimulation sensorielle non-invasive, peu contraignante et potentiellement complémentaire, voire alternative à la pratique physique. Elle pourrait permettre des améliorations de la force musculaire et de l'équilibre sans fournir d'effort ou de contractions musculaires volontaires. Toutefois, l'utilisation des vibrations chez des sujets très âgés et dépendants n'a pas été expérimenté de manière exhaustive. L'objectif de cette étude est d'explorer les effets aigus de différentes durées de VL du tendon quadricipital au repos sur les performances de vitesse maximale de marche et de force du quadriceps. Ainsi, nous cherchons à déterminer si la VL peut être un outil d'entraînement passif complémentaire ou alternatif à l'activité physique. Les participants sont des résidents volontaires de l'EHPAD Marcellin Vollat de Digoin (France, 71) qui ne présentent pas (ou peu) de troubles cognitifs, ostéo-articulaires et neurologiques. L'ensemble des participants ont reçu 4 sessions de VL (3min vibration, 3min sham, 9min vibration et 9min sham) au niveau du tendon quadricipital de manière aléatoire avec une période de washout d'au moins 7 jours. La vitesse maximale de marche sur 10m et la force maximale volontaire isométrique des quadriceps ont été mesurées 5 minutes avant la VL, 5 minutes après la VL, puis 15 minutes minimum après la VL. Les analyses statistiques ont montré que la VL a diminué la vitesse maximale de marche et la force maximale des quadriceps 5min après l'arrêt de la stimulation. Les performances se détériorent d'autant plus que la durée de VL est importante. En revanche, les conditions placebo n'ont pas révélé de différences dans les performances. Exception pour le 9min sham qui semble étrangement lui aussi diminuer la force maximale des quadriceps. Ces durées de VL semblent créer une fatigue musculaire qui pourrait correspondre aux effets d'un entraînement physique. On peut supposer qu'en appliquant une stimulation chronique la force pourrait être améliorée par un meilleur recrutement des unités motrices. La simplicité d'application, l'absence de douleurs ou d'effort lors de la VL pourraient offrir une thérapie de rééducation physique efficace chez des sujets âgés déconditionnés, parfois peu motivés et ayant une mobilité réduite.

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Mots-Clés: Réadaptation physique, vibration locale, neuromusculaire, force, proprioception, personnes âgées

Age related-sex differences in cardiovascular responses to eccentric cycling : preliminary outcomes of the SWEETEXC study

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Résumé

INTRODUCTION
Endurance exercises are well-documented to improve cardiorespiratory fitness that reduces overall mortality, including elderly and pathological populations (Friedenreich et al., 2020; Li et al., 2018). Traditional exercises such as locomotors activities (e.g. walking, cycling) favour mainly the concentric muscle contraction form, that may prevent deconditioned populations from achieving sufficient levels of muscle mechanical tension to promote health effects. Eccentric cycling represents a promising alternative in a clinical context providing the reduction in oxygen uptake compared to conventional concentric cycling for greater muscle stimulation. The characterization of cardiovascular responses during eccentric cycling remains however unexplored, limiting therefore its implementation in clinical context. We hypothesize that the Rate Pressure Product (RPP = Heart Rate*Systolic Blood Pressure) is a reliable easy-to-monitor indicator for prescribing the intensity of eccentric cycling.

METHODS

11 healthy people have so far been included in this study. The first visit was dedicated to determine maximal concentric power on a semi-recumbent seated cycle (Pmax). After familiarisation (4 sessions), eccentric cycling consisted of 5-minute stages at 5 intensities (40%, 55%, 70%, 85%, 100% of Pmax) performed at 40 rpm. A non-invasive blood pressure device (Finapres Medical Systems, Chennai, India) and a 3-lead electrocardiogram were used to collect hemodynamic responses and heart rate, respectively.

RESULTS

The higher the intensity, the greater the hemodynamic responses and heart rate. Both heart rate (100%Pmax : 110.2 ± 8.6 bpm; 70%Pmax : 102.9 ± 10.4 bpm; 40%Pmax : 82.8 ± 12.0 bpm), systolic blood pressure (100%Pmax : 171.6 ± 12.6 mmHg; 70%Pmax : 156.6 ± 16.2 mmHg; 40%Pmax : 149.8 ± 8.4 mmHg), or cardiac output (100%Pmax : 10.5 ± 2.9 L.min-1; 70%Pmax : 10.2 ± 2.2 L.min-1; 40%Pmax : 6.2 ± 0.9 L.min-1) tended to increase with exercise intensity. As a result, RPP showed a similar increase (100%Pmax : 15755 ± 1548 bpm.mmHg; 70%Pmax : 13435 ± 2094 bpm.mmHg; 40%Pmax : 10854 ±

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1434 bpm.mmHg), with no threshold since a linear increase seems to be apparent with the intensity increments (R2=0.988).

DISCUSSION
These preliminary data do not allow further investigation or comparisons between groups. However, eccentric cycling appears to be a safe and tolerated alternative when performed at submaximal intensity. Its consideration in the clinical context may be relevant for population with severely limited exercise capacity.

Mots-Clés: eccentric exercise, cardiovascular function, Rate Pressure Product

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30e EDITION

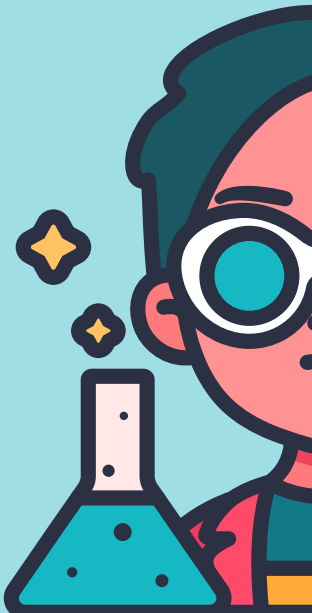
FORUM DES JEUNES CHERCHEURS

DOCTEURS DE DEMAIN

6 juin 2025

SESSION SCIENCES DE L'ENVIRONNEMENT

9:30 - 11:30



Connecting Large-Scale Atmospheric Circulation to Spring Frost Events in Marlborough Vineyards

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Résumé

Spring frost events pose a significant risk to viticulture. In Marlborough, New Zealand's leading wine region, the economy is heavily dependent on vineyard yields, making spring frost events a critical threat.
Climate change exacerbates this risk, as the increase in warmer temperatures has led to the advancement of phenological stages in grapevines, like bud break, exposing vines to potential late frost events. Despite these implications, frost risk in Marlborough has not been thoroughly assessed since 2018, emphasizing the need for an updated analysis.

Initial research on frost occurrence patterns was conducted in 2009 and revealed significant variations in observed climate across New Zealand's primary vineyard regions. This suggests that temperature changes are not uniform throughout the country, with Marlborough experiencing an increase in frost occurrence in contrast to other areas. These regional disparities have been attributed to changes in large-scale atmospheric circulation and its interaction with New Zealand's complex topography.

Given the high sensitivity of the wine industry to weather fluctuations and the considerable regional variability in trends of key parameters, such as temperature, a deeper understanding of the spatial and temporal variability of New Zealand's weather regimes is proving to be highly valuable for viticulture.

This study investigates the variability of spring frost events in Marlborough by linking large-scale atmospheric circulation patterns to local climate impacts.

We use Self-Organizing Maps (SOMs) to classify weather regimes based on daily mean sea level pressure (MSLP) fields from ERA5 reanalysis (1940-2022), with future extensions incorporating geopotential height. Unlike traditional clustering methods, this approach preserves the continuum of atmospheric variability and captures transitional states, offering a robust framework to analyse synoptic-scale circulation.

To assess frost distributions across the Marlborough vineyards, high-resolution (1km) WRF model data are used. Identified frost days are then linked to the corresponding SOM regimes. This highlights the recurrence and dominance of specific circulation types associated with frosts.

The proposed methodology aims to elucidate the large-scale and synoptic drivers of frost

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events by exploring their spatial and temporal distribution with fine precision. The results identify the role and recurrence of specific circulation patterns, responsible for triggering spring frost events.
By improving the identification of weather patterns responsible for frost events, this research sets the groundwork for developing targeted frost risk forecasts and management strategies, ensuring resilience in the face of climate change for the New Zealand wine industry.

Mots-Clés: Weather Regimes, Grapevines, Frost, Atmospheric Circulation

Effect of soil water content on soil respiration sensitivity to temperature (Q10) in a temperate beech forest: overview of data processing from four years of observation with automatic chambers

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Résumé

Soil respiration (RS) is the primary source of atmospheric carbon dioxide from terrestrial ecosystems. RS has been shown to respond exponentially to temperature, a relationship summarized by the Q10 parameter, which quantifies the increase in RS with a 10∘C rise in temperature. Q10 depends on both temperature and soil water content, but the latter's effect on RS and Q10 remains unclear, especially in temperate forests. Unlike soil temperature, whose influence on RS is widely accepted, soil water content's effect is more site-due to multiple factors such as land use, soil and climate characteristics. Continuous, high-frequency field data are needed to improve understanding, but such data are challenging to collect in forest environments.
Here, we question the effect of soil water content on Q10 along the annual cycle in a temperate deciduous beech forest. Do soil water content levels have an impact on Q10 values? Is the relationship between soil water content and Q10 the same throughout the annual cycle? The experimental site is located in the Châtillonnais National Forest Park in the North-Eastern part of France. There, RS and environmental parameters are measured hourly using 4 automated chambers (LI-8100, LI-COR) since 2020 (4-year dataset). The forest has been protected from harvesting for over 30 years and is classified as an integral biological reserve.

The dataset includes over 145,000 RS measurements with about 6.1% missing data. After quality control and outlier removal, 92.7% of the data are used for analysis. For each hour, the mean RS is calculated by fitting exponential and linear models, with the best model selected based on AIC (ResChamberProc package in R developed by Wutzler T.). RS values are considered reliable when the coefficient of determination exceeds 0.9. Soil water content, measured near each chamber, shows high temporal consistency but high magnitude spread due to heterogenous soil conditions. To standardize, values are normalized by dividing each by the maximum recorded value, creating bins from 0 (dry) to 1 (wet).
We found that Q10 can only be calculated for spring and autumn (2.71 and 3.12 respectively) in our study site. During winter, low temperatures prevent meaningful Q10 calculation, while in summer, dry soil conditions limit results. A threshold analysis revealed that soil water content positively affects Q10 when it exceeds 40% of the maximum value. This indicates that RS is much more temperature-sensitive in wet than dry soils.

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Mots-Clés: Soil respiration, Q10, Soil moisture, Processing, Modelling

Exploring the Diversity, Evolution and Genetic Determinism of Specialized Metabolites in Pea (Pisum spp.) Seeds

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Résumé

Pea (*Pisum sativum* L.), the most important legume crop cultivated in France, produces protein-rich seeds that are increasingly used as a source of protein for food applications. However, pea seeds accumulate specialized metabolites (SM) that can modify the organoleptic properties of the protein fractions and affect their functional properties, while others play a physiological role and give an essential contribution to seed's defense against environmental stresses, highlighting the need to take this dual role into account in breeding programmes. Despite their importance, the genetic and biochemical bases of SM biosynthesis in pea seeds remain poorly understood, and the study of their diversity has been neglected. To fill this gap, we performed untargeted metabolomic analyses (LC-MS/MS) on mature dry seeds, separating seed coats and cotyledons, from a diversity panel of 204 pea genotypes, comprising wild and domesticated Pisum species and subspecies, as well as widely cultivated varieties.

The results obtained for the seed coats, the protective tissue surrounding the seed, reveal a high metabolic diversity and clear metabolic specificity between species and subspecies, underlining the impact of evolutionary processes and domestication on seed coat chemical defences. To identify the genetic basis of these traits, a metabolomic genome-wide association study (mGWAS) is currently being conducted to pinpoint candidate loci and genes involved in the biosynthesis, modification and/or regulation of agronomically relevant SM. As a case study, we performed a GWAS on pisatin, an isoflavonoid phytoalexin known to be produced in response to abiotic stress, which led to the identification of a significant association peak on chromosome 3. Further investigations are underway to characterize the

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underlying genetic determinants.
These findings shed light on the complex metabolic landscape of pea seed coats and open new avenues for understanding their role in adaptation, defense, and domestication.

Mots-Clés: Legumes, Seed, Quality, Metabolome, Environment, GWAS

Flux de carbone et d'eau dans un écosystème viticole face au changement climatique

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Résumé

Les professionnels de la filière viticole de Bourgogne et Champagne se sont engagés à participer à l'atténuation du changement climatique (i.e., atteindre la neutralité carbone d'ici 2035/2050) et doivent en parallèle s'adapter à l'intensification des aléas climatiques. Pour répondre à ce double enjeu, la mesure des flux de carbone (NEE) et d'eau (ET) dans l'écosystème viticole est indispensable afin de caractériser la dynamique temporelle de ces flux et de comprendre l'influence du climat (e.g., vagues de chaleur et sécheresses) et des pratiques culturales (e.g., labour, enherbement et gestion des sarments) sur cette dynamique. En particulier, les attentes sont fortes pour identifier les pratiques favorisant le stockage de CO2 tout en limitant les risques de stress hydrique. Une tour à flux a été installée en juin 2024 dans une parcelle viticole à Rully (Saône-et-Loire) afin de quantifier les échanges de carbone et d'eau entre cet écosystème et l'atmosphère. Elle permet d'estimer ces flux en combinant un anémomètre 3D et un analyseur à haute fréquence (10Hz) selon la méthode eddy-covariance et de relier leur dynamique temporelle aux conditions climatiques locales et aux pratiques. Cette tour permet également de calibrer un modèle sol-plante-atmosphère (STICS), outil indispensable pour extrapoler les résultats à d'autres terroirs, mener des expériences de sensibilité pour identifier la combinaison optimale de pratiques et projeter l'évolution des flux de carbone et d'eau au cours du 21ème siècle.

Mots-Clés: Carbone, Eau, Viticulture, Climat, Eddy, Covariance, Modélisation

*Intervenant

DESIGNING A COLLECTIVE PLAN FOR ADAPTING FARMING PRACTICES AND PROTECT THE DRINKING WATER QUALITY IN A SMALL DISTRICT IN EASTERN FRANCE

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Résumé

CONTEXT **:** Drinking water quality has been negatively impacted by agricultural intensive use of pesticides and nitrogen over the past 50 years. In France, 1,000 drinking water catchments must be protected under the national Ecophyto plan. Since 2010, local authorities delivering drinking water to inhabitants must compulsory develop and implement action plans to reduce such pollution (Ministère du Travail, de la Santé, des Solidarités et des familles 2024). In the south of Territoire de Belfort department (Eastern France) two of eight water catchments must be compulsory protected because of pesticides contaminations, while other water catchments are also contaminated. Molecule responsible for contamination is mainly S-métolachlor, an herbicide in maize crop no longer approved in France since 2024. This agricultural model is also threatened by climate change which could impact crop production in the coming years. In this context, a participatory research project is undertaken since December 2024 to contribute to the reduction of drinking water pesticides contamination at the territory scale, while facing climate change and preserving the economic performance of farmers.
OBJECTIVES : The main issue of the study is to develop and implement a collective change in farmers agricultural practices, using participatory research and modelling process to co-design agricultural systems, that preserve sustainably water quality.
METHODS and PERPECTIVES : Participatory research combining co-design of farming system is a valid approach to enhance dynamic change in farmers practices (Meynard, Dedieu, and Bos 2012; Gouttenoire, Cournut, and Ingrand 2013; Barataud et al. 2014). This approach requires a depth knowledge of farming practices, but also social, economic and ecological interactions between stakeholders involved in water quality protection (Barataud et al. 2014; Duru, Therond, and Fares 2015). This co-design process requires supporting tools, like models to explore and assess solutions during design (Queyrel et al. 2023). Our method begins by farmers semi-directed interviews, to identify the diversity of agricultural practices, global constraints, and technical-economic and environmental performances. Second step is to organise workshops on cropping systems design with farmers and stakeholders. Third step is to modelling impacts of emergent cropping systems on various aspects: economic performance, pesticides transfer risk to groundwater, impact of climate-change, etc. Finally, the purpose of this co-design process is to provide a set of technical and economic references for farmers and agricultural firms to initiate concrete changes and foster a collective dynamic.

*Intervenant

Mots-Clés: Participatory research, water quality, agricultural practices, weed

Understanding soils in fruit agroforestry systems: impact of the presence of service plants on soil functions, microbial communities and root systems of fruit trees.

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Résumé

Fruit production systems are heavily impacted by several factors: global climate change leading to extreme weather events and pressure on water resources, volatile costs of raw material, accelerated emergence of new bio-aggressors coupled with progressive banning of pesticides... In this context, applying the principles of agroforestry to fruit production could be a way to improve orchard's sustainability. This involves interplanting perennial vegetation between, or around, fruit trees, as a potential provider of services in terms of biodiversity, soil fertility, plant health, resilience towards extreme climatic events... Such fruit agroforestry systems are inspired by pre-existing agroforestry practices such as syntropy, successional agroforestry in the tropics, or from garden-forests, hedgerow-orchards in temperate areas... Yet, there is a lack of knowledge on how plant species interact with each other and with the soil.

To better understand these interactions, an experimental mesocosm design was installed in a greenhouse in 2024, consisting of pear trees planted in jars with or without perennial service plants. The companion plants were chosen for their rapid growth and high capacity to produce biomass. These were either pruned, with the biomass returned to the soil, or left unmanaged for the season. The idea was to see how the management of companion plants affects soil functioning, root system development and pear tree growth. To do so, some biological parameters (soil enzymatic activity, mycorrhizal colonization, microbial respiration), and tree growth (trunk diameter, branch length) were assessed over time starting in March 2024. In addition, labile carbon and mineral nitrogen were measured at the beginning of 2025.

The main results show that in presence of companion plants, pear trees exhibited delayed growth, partially compensated by the restitution of organic matter. Regarding soil functioning, in most cases enzymatic activities were higher when companion plants were present, suggesting an increase in biological activity – but this result was not maintained throughout all assays. Mineral nitrogen tended to be higher under the form of ammonium but lower in nitrate in presence of companion plants, as compared with the control.

Implementing service plants in orchards has great potential for improving the biological functioning of the soil. However, initial results show that, in association with companion plants, competition for resources is high, especially when these are left unmanaged. This competitive effect could be reinforced by the space constraints imposed by pots. Further data will be acquired to assess the impact of these plants on soil fertility.

*Intervenant

Mots-Clés: Fruit Agroforestry, Soil functioning, Roots systems, Syntropy

Weed perception and management decision criteria of farmers reducing reliance on herbicides

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Résumé

Economic weed thresholds refer to the density of a specific weed species in a particular crop, beyond which the cost of yield loss caused by the weed exceeds the cost of herbicide application. It is the main indicator to trigger a herbicide treatment. Economic thresholds are commonly used to assess the harmfulness of weed species since the 1970s. However, with the national and international objectives of reducing reliance on herbicides and the promote of integrated weed management, new research approaches focusing on weeds' functionality have emerged. Weeds are no longer viewed solely as pests but are also evaluated for their potential to provide ecosystem services. They are no longer measured on a species-by-species approach, but described as plot-specific communities filtered through the cropping system and landscape. Farmers who reduce the reliance on herbicides face new challenges in assessing the potential harmfulness of weeds and deciding to act with a wide range of tactics. We therefore aimed to study farmers' perception of the negative and positive effects of weeds and their management decision criteria when implementing integrated weed management (IWM). We conducted a survey of Swiss arable farmers in winter 2023. In total, 562 farmers responded, with a representative distribution across Switzerland's agricultural regions. 13% of the respondents were organic farmers, 70% subscribed to a federal contribution for pesticide reduction and 35% subscribed to a federal contribution for herbicide reduction. The median number of crops per farm was six, with a predominance of wheat, maize, temporary meadow, rapeseed and barley. The most problematic weeds cited were perennial species (e.g. *Cirsium arvense*) and grass species (e.g. *Echinochloa crus-galli*). The indirect effects of weeds (e.g. increased soil seed bank) are perceived as more important than the direct effects (e.g. yield loss). Weed observation remains a predominant criterion for decision-making (93% of farmers) but the decision criteria are not based on weed density but the presence of specific weed species and their growth stage in relation to crop development. Indicators, such as the number of weed species or evenness between species, are rarely taken into account by farmers. This suggests new avenues of research to provide farmers with relevant indicators to help them implement IWM.

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Mots-Clés: integrated weed management, weed perception, decision criteria, weeds, arable crops, survey

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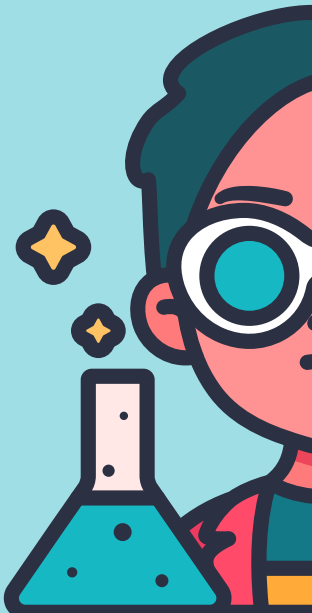
SESSION NEUROSCIENCES

13:30 - 15:30



Role of the lingual GLP-1 system in sweet taste detection

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Résumé

Background. Sweet taste perception is mediated by the T1R2/T1R3 receptor expressed in taste cells of the tongue. This receptor responds to a wide range of sweet compounds, including sugars or artificial sweeteners. In mice, genetic deletion of T1R2/T1R3 significantly reduces attraction to sweet substances and alters central processing of gustatory signals. However, a residual behavioral response to glucose persists, suggesting the involvement of an alternative glucose-sensing mechanism within the taste system. The incretin hormone glucagon-like peptide 1 (GLP-1), known to be secreted by intestinal L-cells in response to nutrient intake and to have a role in glucose homeostasis, and its receptor, have been located in taste cells. However, their functions within the gustatory system remain largely unexplored.
Objective and Methods. The aim of this study was to investigate the role of GLP-1 in modulating sweet taste sensitivity in mice. Virogenetic silencing approaches were employed to specifically reduce the expression of the GLP-1 receptor (GLP-1R) in the tongue of adult C57BL/6J mice. Behavioral responses were then assessed using a brief-access taste test in a gustometer. A series of different sweet solutions is presented to the mouse in 10-second trials in a randomized order within a block across a 20-minute session. Because of the short duration of each trial, this test explores the behavioral responses to gustatory cues by minimizing post-ingestive effects. In the first assay (Glucose vs. Fructose, GvF), mice were given access to glucose and fructose solutions at three concentrations (0.316 M, 0.56 M, 1.1 M). Subsequently, mice were exposed to increasing concentrations of glucose alone, then fructose alone.

Results. In the GvF test, a significant difference in licking responses was observed between glucose and fructose at the intermediate 0.56M concentration in GLP-1R knockdown (KD) mice. In the fructose-only test, GLP-1R KD mice exhibited increased licking responses to 0.56 M fructose compared to control mice, while no apparent effect on licking behavior was observed in the glucose-only test between the groups.

Conclusion. Virogenetic silencing of GLP-1R in the taste system appears to modulate the ability of mice to perceive fructose at an intermediate concentration, suggesting a role for the GLP-1/GLP-1R system in modulating sweet taste sensitivity.
Perspectives. Further studies will assess the impact of GLP-1/GLP-1R signaling in T1R2/T1R3 knockout models to better understand its role in taste detection without the canonical sweet information. In addition, the potential involvement of lingual GLP-1 in systemic glucose metabolism will also be investigated.

*Intervenant

Mots-Clés: Sweet taste perception, T1R2+T1R3, Glucose sensing, GLP 1, Tongue

Loss of physiological postprandial microglial reactivity in aged mice

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Résumé

Background. An inflammatory response occurs after consuming a meal. Recently, the team demonstrated that the postprandial inflammatory response takes place not only at the peripheral level but also in the brain, particularly in the hypothalamus, an area that controls food intake. This response involves the activation of microglial cells, the immune sentinels of the brain, that adopt a hyper-ramified shape associated to a pro-inflammatory phenotype. This response is specific to the nutrients and occurs after a high fat meal, but not after a balanced meal. This response has a homeostatic function as it promotes satiety. One possibility is that the adaptive postprandial response could be loss or altered by the chronic inflammatory state of the brain during aging, which might explain the installation of eating behavior disorders in the elderly.
Objectives and Methods. The aim of the project is to explore whether the microglial inflammatory signaling still occurs after a meal during aging. To assess it, we performed microscopic characterization of the postprandial microglial response in old (20.5 months) versus young (2.5 months) males mice according to the prandial state. Mice received no food, or a standard diet or a high fat diet during 3 hours. Brains were collected and prepared for histology. Morphology of microglia was analyzed by immunolabeling, confocal imaging and 3D reconstruction. To correlate results with the metabolic state, body composition and feeding behavior were also assessed.

Results. As expected, aged mice exhibited high body weight, increased lean mass and decreased fat mass. Food intake analysis showed that aged mice were hyperphagic. Morphometric analysis of microglia in the arcuate nucleus of the hypothalamus of mice exposed to a high-fat diet (3h) revealed that the postprandial microglial response was lost in aged mice.

Conclusion. We found that elderly male mice did not initiate postprandial microglial reactivity after a fatty meal, contrary to that observed in younger mice. The absence of the postprandial microglial response that promotes satiety in young mice might explain the observed hyperphagia of the aged mice on HFD.
Perspectives. It would be interesting to test whether the anti-aging effects of long-term caloric restriction could restore the postprandial inflammatory response. To that end, an anti-age intervention consisting in 20% long-term caloric restriction on mice (from 6 to 20 months) has been set up.

*Intervenant

Mots-Clés: food intake, microglia, brain, aging, inflammation, energetic homeostasis, eating behavior

Isolating implicit and explicit processes during visuomotor adaptation

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Résumé

Introduction: Visuomotor adaptation relies on two distinct processes: explicit (conscious, intentional) and implicit (unconscious, automatic), which operate together to minimize errors and ensure accurate movements. Many studies have recently tried to isolate the two processes under different conditions, such as age(1) or mental fatigue(2) , and found a competitive interaction between these two processes. Although other factors, such as time-of-day, are known to influence motor learning(3), their effects on motor adaptation, particularly on explicit and implicit components, remain unclear. In this study, we investigated the potential diurnal fluctuations of visuomotor adaptation when implicit (Experiment 1, Exp.1) and explicit (Experiment 2, Exp.2) components were isolated.
Method: Participants (Exp.1 n=30; Exp.2 n=34) performed a 45◦ visuomotor adaptation task, either at 10 am (morning) or at 3 pm (afternoon). In Exp.1, participants performed 480 'clamped visual feedback' trials to isolate the implicit component. In Exp.2, we isolated the explicit component using the 'delayed visual feedback' method through 128 trials. For both experiments, the adaptation session was divided into early and late adaptation phases, representing, respectively, the beginning (40 trials) and the end (40 trials) of the adaptation. We mainly analyzed the early phase of adaptation (i.e., until maximum adaptation was reached) since it is during this phase that adaptive changes occur.

Results and discussion: A two-sample t-test revealed no significant differences between groups during the early phase of adaptation. Interestingly, our previous work showed that when both components are expressed simultaneously (i.e., during a classical adaptation paradigm), the speed of adaptation and the explicit component are affected in the morning. Further investigations are necessary to clarify the underlying mechanisms.

(1) Elizabeth Cisneros et al., " Differential Aging Effects on Implicit and Explicit Sensorimotor Learning ", 4 juillet 2024

(2) David Apreutesei et Erin K. Cressman, " The Effects of Mental Fatigue on Explicit

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and Implicit Contributions to Visuomotor Adaptation ", *PloS One* 19, no 8 (2024)

(3) Charlène Truong et al., " Time-of-Day Effects on Skill Acquisition and Consolidation after Physical and Mental Practices ", *Scientific Reports* 12, no 1 (8 avril 2022)

Mots-Clés: Visuomotor adaptation, Implicit process, Explicit process

Investigating the Blood-CSF Barrier in Alzheimer's Disease: Aβ Transport and Barrier Integrity

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Résumé

Alzheimer's disease (AD) affects around one million people in France, which underscores its significance as a major public health issue. To date, no treatment currently accessible on a large scale has proven effective in slowing, curing, or preventing the severe cognitive impairments associated with this neurodegenerative condition. Besides, the underlying neurobiological mechanisms of AD remain largely misunderstood. AD is characterized by the presence of extracellular plaques of amyloid-β (Aβ) peptide aggregates, and intracellular deposits of hyperphosphorylated Tau protein (pTau), forming neurofibrillary tangles. The physiopathology of AD is also linked to blood-brain barrier (BBB) alterations. The Aβ peptide exchange mechanisms between the blood and the brain are multiple and bidirectional, and the accumulation observed in AD patients partly results from an impaired brain clearance involving various BBB transport mechanisms. Clinically, pTau and Aβ proteins are also found in the cerebrospinal fluid (CSF), reflecting the role of the blood-CSF interface and the blood-CSF barrier (BCSFB) in the cerebral clearance of these toxic molecules. Moreover, the expression of certain transporters involved in the cerebral Aβ peptide clearance has been shown altered in human ependymal cells and/or choroid plexuses, suggesting that these BCSFB elements play a key role in the development of AD. We believe that some BBB receptors also present in the BCSFB may play an important role in Aβ accumulation. My doctoral research therefore focuses in investigating the underlying mechanisms assuring the integrity of BCSFB, through the analysis of the expression of Aβ transporters and tight junction proteins responsible for maintaining barrier impermeability. To overcome the lack of knowledge about the effects of AD on the BCSFB, we use cutting-edge methodology such as

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tissue clearing, laser microdissection, and ddPCR, to allow for a more precise comparative analysis of the barrier's anatomo-functional components. Our work has already demonstrated the applicability of tissue clearing and laser microdissection for the study of choroid plexuses. Our preliminary results also show an increased gene expression of the Aβ peptide influx LRP-1 receptor in the choroid plexuses of an AD transgenic mice model (3xTgAD) compared to control mice. Overall, our first findings suggest that our methodological approach will provide valuable data for a better understanding of AD and its relationship with the BCSFB. It is now crucial to apply these methods to a broader range of Aβ peptide transporters and tight junction proteins.

Mots-Clés: Alzheimer's disease, amyloid, β, blood, brain barrier, blood, CSF barrier, choroid plexus

Behavioral Impact of Volatile Compounds on Drosophila Species and Involvement of a Complex Sensory Detection Pathway

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Résumé

Global warming, along with international trade and human movement, has contributed to the spread of insect pests such as *Drosophila suzukii* in France. In this context, we have recently observed striking effects of two volatile compounds-propanoic acid and butyric acid-not only on the behavior of this invasive species but also on the model organism *Drosophila melanogaster*. These acids attract larvae but strongly repel adults, significantly altering courtship behavior and leading to the complete suppression of copulation. At higher concentrations, they also induce anesthesia in adults (patent PCT/EP2020/075386). The mechanisms underlying the detection and action of these compounds remain largely unknown. Classical chemosensory organs such as the antennae appear to be only partially involved, raising a new question: could an alternative sensory pathway be mediating the perception of these acids? Recent findings suggest the possible involvement of a previously unidentified olfactory organ. Through combined genetic and behavioral approaches but also neuroanatomical analysis, our objective is to inverstigate the molecular and anatomical basis of this perception in order to develop ecological, non-toxic strategies for fruit crop protection that are compatible with biodiversity conservation and human health.

Mots-Clés: Olfaction, Neurobiologie, Génétique, Evolution, Reproduction, Parade

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Protocole expérimental d'une étude de faisabilité sur l'impact de l'activité physique sur la qualité du sommeil de personnes présentant un trouble de l'usage d'alcool

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Résumé

Contexte

L'usage d'alcool détériore la qualité du sommeil et dérègle l'horloge centrale. La présence d'insomnie en amont des consommations excessives d'alcool est fréquente et la persistance de celle-ci à l'issue d'un sevrage augmente les rechutes tandis que son traitement améliore l'abstinence. Ainsi, le traitement du mésusage d'alcool ne peut être envisagé séparément de la prise en charge du sommeil. Or, l'Activité Physique Adaptée (APA) permet de lutter contre l'addiction. De surcroit, l'exercice est un puissant Zeitgeber(1) qui a un impact positif sur la qualité du sommeil dans la population ordinaire. Néanmoins, peu d'études investiguent l'impact de cet outil sur le sommeil de cette population spécifique. Ce manque de publication pourrait être expliqué par le risque d'abandon accru parmi la population étudiée. C'est pourquoi ce protocole de recherche a pour objectif d'investiguer la faisabilité de la mise en place d'une étude évaluant l'impact de l'activité physique sur le sommeil de personnes présentant un trouble de l'usage d'alcool.

Méthode

Ce protocole vise à étudier 40 sujets (18 – 65 ans), de l'Hôpital de jour d'Addictologie de Besançon, présentant une plainte de sommeil et un trouble de l'usage d'alcool. Tous les sujets réaliseront trois entretiens, à l'inclusion, au milieu du programme de 12 semaines et à la fin de l'étude. Ces entretiens comprendront un examen clinique, des analyses (éthylotest, prélèvement sanguin), la passation de questionnaires (sommeil, activité physique, dépendance à l'alcool, qualité de vie...) et l'évaluation des capacités physiques et de la motivation. Le sommeil des sujets sera évalué objectivement pendant 2 semaines, avant et après le programme (actimétrie, agenda du sommeil, mélatonine urinaire). Les sujets seront randomisés en deux groupes. 10 dans le groupe autonome qui recevront une brochure de recommandations. Les 30 sujets du groupe encadré bénéficieront de trois séances hebdomadaires, matinales, d'une heure, d'APA. Les séances collectives comprendront des efforts aérobies et

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anaérobies, d'intensité modérée à élevée. Tout au long de l'étude les sujets rempliront un agenda de suivi des consommations d'alcool et un calendrier de suivi des pratiques physiques.

(1) Synchroniseur de l'horloge centrale

Mots-Clés: Activité Physique, Sommeil, Alcool, Protocole, Addiction

From Booster to Breaker: Chronic EMS Dampens Hippocampal BDNF and Promotes Neuroinflammation

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Résumé

Physical exercise (EX) is the most effective non-pharmacological strategy for promoting health, preventing diseases, and aiding rehabilitation in stroke, depression, or neurodegenerative disorders (Mandolesi et al., 2018). Its benefits are largely mediated by brain-derived neurotrophic factor (BDNF), a key regulator of neuroplasticity and neuroprotection. The critical role of BDNF is evident, as anti BDNF strategies abolish EX-induced cognitive benefits (Vaynman et al., 2003). Recent findings highlight an endocrine dialogue between the brain and contracting muscles, where myokines secreted into the bloodstream stimulate cerebral BDNF synthesis. However, vulnerable populations (e.g., elderly, stroke, COPD or heart failure patients) may have limited capacity to engage in traditional EX. For individuals unable to perform dynamic exercise, electromyostimulation (EMS) - a transcutaneous peripheral electrical stimulation - emerges as a potential alternative to counteract cognitive decline and support brain health. Our team previously demonstrated that acute EMS (two sessions, one week apart) enhances cognition in humans and neuroplasticity in animals via muscle-brain humoral interactions (Chaney et al., 2024). To amplify these benefits, we applied a chronic EMS protocol (7 days, 30 minute/day; 40Hz frequency, 400μs pulse width, 7s ON/14s OFF, progressive intensity: 6-20mA) on 8-week-old Wistar rats. Unexpectedly, chronic EMS disrupted hippocampal BDNF signaling, reducing neuroplasticity-related proteins. As assessed by several cognitive tests, this protocol also induced anxiety-like and depressive-like behaviors. At the muscular level, EMS induced tissue damage and elevated pro-inflammatory cytokines, with increased serum corticosterone. This heightened inflammatory response extended to the hippocampus, where EMS-treated animals exhibited exacerbated neuroinflammation. These findings reveal a dualistic nature in muscle-brain crosstalk and underscore the need to optimize EMS protocols for individuals unable to engage in conventional physical activity.

Mots-Clés: BDNF, Exercise, Electromyostimulation, Muscle, Cognition

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Influence of motor imagery on behavioral inhibition

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Résumé

Introduction

Motor imagery (MI) is the mental representation of a gesture without the concomitant production of movement. During MI, brain-muscle excitability is increased. This activation of the sensorimotor system is accompanied by inhibitory mechanisms within the primary motor cortex, to prevent movement when the person imagines an action.

However, it is not clear from the literature whether MI involves specific or identical inhibition to the behavioral inhibition involved in the control of real actions. Moderate-intensity physical activity training has been shown to improve proactive inhibition (inhibition upstream of motor command, measured by a Go/NoGo task) and reactive inhibition (inhibition of a current action, measured by a Stop-Signal task), To date, it has not been established whether imagery training would alter these behavioral inhibition abilities.

The aim of this study is to test whether a short session of real or imagined repetitions of sequential finger movements can modify behavioral inhibition capacities.

Methodology

To date, 17 healthy volunteers out of 66 planned have been included. Participants were divided into 3 groups (IM, Physical Activity, Control) who performed an imagined manual sequence task, an actually performed manual sequence task and an attentional activity (5 blocks of 10 trials), Respectively.

In pre- and post-test, participants performed 2 behavioral tests aimed at assessing proactive inhibition (Go/NoGo), and reactive inhibition (Stop-Signal).

Results

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For the measurement of proactive inhibition (Go/NoGo), the dependent variable is the difference between the reaction time to the block containing only Go trials and the reaction time from Go trials to mixed blocks (Go and NoGo trials).

For the measurement of reactive inhibition (Stop-Signal), the dependent variable is the Stop-Signal Reaction Time (SSRT). It corresponds to the latency of the stopping process.

We will perform a repeated-measures Anova including a within-subject TEST factor (pre-post) and a between-subject GROUP factor (MI, Physical Activity, Control) in order to highlight any differences between our groups in the evolution of behavioral inhibition.

Discussion

We plan to include 49 new participants in the 3 groups. If MI involves inhibition mechanisms similar to behavioral inhibition, a short mental training session should modify proactive and reactive inhibition variables.

Conclusion
These results have to be confirmed with a bigger sample. A future application of this thesis work is the implementation of a motor imagery protocol with a public suffering from chronic pain. Our aim is to stimulate inhibition capacities in order to create plasticity and re-engage movement.

Mots-Clés: Inhibition, motor imagery

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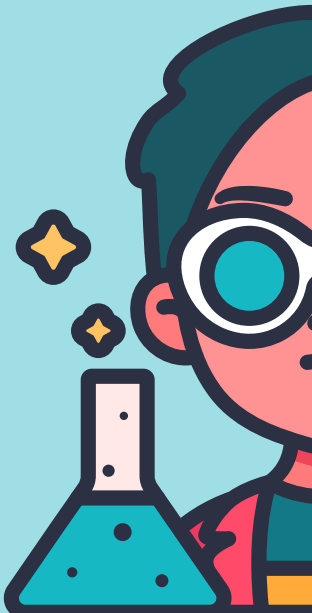

Characteristic and enhancement aroma profile of rice wine produced from non-cooking process.

Profil aromatique caractéristique et enrichissant du vin de riz produit à partir d'un procédé de production sans cuisson

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Not only in Vietnam but also in other Southeast Asia countries, in the traditional rice wine production process, begin with the pretreatment of the rice by cooking (liquefaction) and preparation of fermentable sugars (also known as saccharification stage) for the yeast to be able to use are the most labor-intensive operation and account for nearly 30% of total costs. With the advances in biotechnology and the development of enzymes for cold starch hydrolysis (CSHE), raw rice starch is transformed into portable ethanol in a one-step process, in which are combined the conventional processes of liquefaction (95-105°C), saccharification (60-62°C), and fermentation (30-32°C) to alcohol in one single bioreactor at ambient temperature. This new process skips rice soaking and cooking procedures, requires low energy, and provides stable ethanol yield. At present, this process has achieved good economic and social benefits in alcohol production. However, it is not widely used due to the unmet demand of consumers for a rice wine with a favorable taste and aroma. In order to solve the problem of single aroma of rice wine production by non-cooking technology, several experimental methods are carried out in the present study. To understand the characteristic aroma profile of rice wine produced from this new technology and to improve its aroma profile by studying different exotic rice varieties and different types of microorganisms integrated, volatile compounds of rice wines were analyzed using gas chromatography-mass spectrometry (GC-MS) combined with headspace solid-phase microextraction (HS-SPME). A total of 35 aroma active compounds were identified and quantified, including 7 alcohols, 18 esters, 3 aldehydes, 3 alkenes, and 1 ketone, which all contribute to the complexity of the aroma profile of rice wine, of which 17 compounds were reported in famous Chinese rice wine and Japanese *Sake*. The aroma profile of non-cooking rice wine suggested giving minimal off-notes, higher levels of higher alcohols (such as isoamyl alcohol, phenylethyl alcohol), and a low level of esters in comparison to other traditional rice wines with more complex and diverse aromatics. Later on, the assessment of aroma profile of non-cooking rice wine using different types of rice varieties (glutinous and non-glutinous) employed with multivariate statistical analysis was carried out, it indicated that esters and alcoholic aroma in rice wine produced from glutinous rice was more prominent than the one fermented with non-glutinous one. Further sensory evaluation is needed to determine the correlation between the aroma compounds and sensory attributes.

Key words: *rice wine, non-cooking process, aroma characteristic, HS-SPME/GCMS analysis.*
Mots clés: *vin de riz, procédé sans cuisson, caractéristique aromatique, analyse SPME/GCMS.*

Towards the optimization of pea nodulated root system architecture for improved water and nutrition acquisition

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Résumé

Grain legumes like pea can meet their nitrogen (N) demands through symbiotic nitrogen fixation (SNF) in root nodules in interaction with soil bacteria Rhizobia, making them a source of N for low-input agrosystems. However, pea growth and yield are sensitive to drought events which have increased incidence due to climate change. Drought associated soil water deficit impairs SNF and uptake of nutrients such as sulfur (S) which is a key element for pea growth, seed protein formation and SNF. In particular, S is a constituent of proteins crucial for SNF: nitrognenase and leghemoglobin and of antioxidant glutathione involved in drought mitigation. Besides, reduced S emissions and deposition due to reduced greenhouse gas emissions has led to S deficiency in cropping systems. An experiment was conducted to understand the impact of water stress (WS S+), sulfur deficiency (WW S-) and their combination (WS S-) on pea growth and hydromineral acquisition with a structural functional analysis focusing on the link between root architecture and hydromineral nutrition. Traits for pea growth and development, nodulated root system architecture, nutrient uptake and allocation were studied in genotypes Kayanne, Cameor and 2684 (lacking vacoular sulfate transporter gene SULTR4) in cylindrical rhizotrons called RhizoTubes. We found that water stress strongly impacted plant ecophysiological traits compared to sulfur deficiency while responding similarly to double stress. Furthermore, all genotypes showed conservative mechanism of reduced shoot and nodule growth while increasing biomass and C allocation to the

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roots to maintain root growth for hydromineral acquisition.Cameor roots increased convex hull but decreased projected area at the bottom of the root length. While both Kayanne and Cameor produced smaller nodules, they were able to maintain nodule metabolism. Kayanne increased nodulation to maintain plant N concentration, while Cameor showed reduced N concentration likely due to increased nodule senescence.Furthermore, decreased S concentration, besides P, K, Mg, Mo and B concentration aligns with water deficit induced decrease in mineral uptake and explains the stronger impact of WS S+ than WW S- which particularly affected nodule biomass caused by smaller nodule size, and reduced N, P, Mo and B concentration. Despite increased S concentration, lower shoot growth and increased root: shoot ratio suggests critical role of S remobilization even under optimum conditions. This also reflects plant attempting to compensate for impaired S mobilization by increasing S uptake through the roots. Furthermore, increased nodule senescence suggests S starvation in the nodules due to impaired sulfate transport.

Mots-Clés: legumes, symbiotic nitrogen fixation, drought, sulfur deficiency, root architecture, ecophysiology

Diversity of metabolic impacts on volatile compounds of Lactic Acid Bacteria in cucumber fermentation

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Résumé

Vegetables are easily perishable, leading to food waste and economic loss. Lactic acid fermentation for vegetables could be a best alternative solution for extending the vegetables shelf-life and providing more value. However, Lactic Acid Bacteria (LAB) are numerous with variable activity and metabolism during fermentation. By investigating the metabolic impacts happening during fermentation based on volatile organic compounds analysis is a primary solution to developing the acceptant fermented vegetables product in terms of flavor and aroma. The aim of this work was to study LAB metabolic impacts for producing volatile organic compounds during fermentation. Firstly, LAB isolation was conducted from six types of Cambodian vegetable fermentation, which resulted in 161 isolates. After eliminating duplicate isolates by using RAPD-PCR analysis, the isolates were then genetically identified showing ninety-seven strains belonging to eleven different LAB species (*Lactiplantibacillus plantarum, Lactiplantibacillus pentosus, Levilactobacillus brevis, Levilactobacillus namurensis, Lactococcus lactis, Leuconostoc citreum, Limosilactobacillus fermentum, Pediococcus pentosaceus, Weissella cibaria, Weissella confuse,* and *Weissella paramesenteroides*). Five LAB species were selected to ferment with cucumber mashed, which were *L. plantarum, L. pentosus, L. lactis, L. fermentum,* and *P. pentosaceus.* The fermentation was conducted with single inoculation for 24 hours at 37 ^{o}C with three biological replications. After fermentation, volatile organic compounds were analyzed by using HS-SPME-GCMS. The result indicated that LAB fermentation had an impact on volatiles modification by comparing identified volatiles before and after fermentation. Furthermore, the volatiles modification was variable depending on LAB species. Aromatic compounds which might be produced via amino acid metabolism, were highly produced by *Lactiplantibacillus* both *L. plantarum* and *L. pentosus.* However, they were distant in terms of volatile aldehydes and saturated primary alcohols which might be produced via fatty acid metabolism. *L. plantarum* produced the highest aldehydes, while *L. pentosus* produced the highest saturated primary alcohol. *L. lactis* was the main producer of esters including fatty acid ethyl esters and acetate esters. *L. fermentum* produced the highest acetic acid and *P. pentosaceus* produced higher acetic acid, which the two species might use two different ways. *L. fermentum* as the heterofermentative LAB might produce acetic acid via glucose metabolism, whereas *P. pentosaceus* as homofermentative LAB might produce acetic acid from respiration-like reaction.

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Mots-Clés: Lactic Acid Bacteria, Volatile Compounds, Fermentation

Impact of Dairy Industry Processes on *Listeria monocytogenes* Stress Resistance and Virulence

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Listeria monocytogenes, a foodborne pathogen commonly found in the food industry, is responsible for listeriosis. According to the EFSA 2023 report, listeriosis is the fifth most reported zoonosis in the European Union, with an increasing notification rate — the highest since 2007. Due to its persistence in industrial environments, eradicating *Listeria* once it enters the production chain is challenging, resulting in significant economic losses due to the EU's stringent safety standards. In addition, its resistance to extreme environmental perturbations is well known and allows its survival to common processes such as acidification and cold storage, both of which occur in the dairy industry, compromising the microbiological safety of dairy products. The heterogeneity of strains' stress resistance to dairy processes and the impact of these processes on *Listeria*'s virulence remain poorly understood, therefore the aim of our study is to better understand the influence of acidification at pH 4.9 and storage at 4°C of semi skimmed milk on the physiology and virulence of two industrial strains of *Listeria monocytogenes*: Lm14 and 07CEB768LM. First, cultivability loss for both strains in response to the above selected stresses was estimated by plate count according to ISO norm 20976 and showed that both conditions had no significant effect on the cultivability of both strains. Their invasion capacity was then assessed before and after stress in the Caco-2 cell model of infection. Our results were then compared to reported human listeriosis cases for both strains. Finally, the ease of transformation of our strains was evaluated by conjugation between *E. coli* S17 donor carrying pCG-TdTomato plasmid containing *L. monocytogenes lmo2230* specific promoter followed by TdTomato encoding gene. Both strains were successfully transformed and expressed the fluorescent protein. Our preliminary results will allow us, in the next steps of the project, to construct a bank of fluorescent mutants on the basis of identified overexpressed genes in response to the selected processes through transcriptomic analysis via RNAseq. The characterization of mutants' fluorescence emission will lead to the establishment of a relationship between *L. monocytogenes* resistance to dairy industry processes and its virulence with a view of possible integration into new generation predictive microbiology models. The use of biomarkers to predict the impact of acidification and cold storage on the virulence, survival and growth of *Listeria monocytogenes* in milk, will thus finetune microbiological risk assessment in the dairy industry.

Sodium alginate as a potential material for protection and delivery of extremely oxygen-sensitive (EOS) probiotics

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Résumé

Next-generation probiotics (NGPs), defined as "live microorganisms identified on the basis of comparative microbiota analyses that, when administered in adequate amounts, confer a health benefit on the host," have recently gained attention over traditional probiotics due to their unique functions in health and disease management (Martín & Langella, 2019). However, most of these strains are extremely oxygen-sensitive (EOS) probiotics, necessitating innovative encapsulation strategies for their protection and delivery. Using edible macromolecules as encapsulating matrices has been widely used in the pharmaceutical and food industries but still needs to be developed to apply to EOS probiotics (Phùng & Karbowiak, 2024). Sodium alginate (SA) can be a potential material for EOS strains since it has a high oxygen barrier property, as well as a good release profile, only swelling and releasing in the intestinal environment (Phùng et al., 2022). SA is an unbranched natural polysaccharide derived from algae, which is non-toxic, biocompatible, and inexpensive (Raghav et al., 2021). It is composed of monomeric units arranged randomly, β-D-mannuronic acid (M) and α-L-guluronic acid (G). SA has unique gelation properties, relying on electrostatic interaction of G blocks with divalent cations, creating a robust matrix (Hu et al., 2021). This study investigates the impact of molecular weight (MW) and M/G ratio on the functional properties of the SA network to protect and release EOS probiotics. Four types of SA were investigated for viscosity in solutions, oxygen barrier of films, and release profile of beads in simulated gastrointestinal fluid (SGF). Protection capacity was studied on the EOS strain: *Faecalibacterium duncaniae*. Results indicated that the MW and M/G ratio of SA do not impact the oxygen barrier property of SA films but significantly influence the mechanical properties of SA beads, as well as the release profile in SGF. SA with low MW and high M/G ratio (SA LMW-M) exhibited excellent oxygen barrier properties and an optimal release profile, dissolving completely in the SGF within 24 hours. In addition, the incorporation of an additive (sucrose) into the SA LMW-M matrix increased *the survival rate of F. duncaniae* during the freeze-drying stage (from 10^5 to 10^7 CFU/mL) and after 2 hours in SGF (from 0 to 10^6 CFU/mL). In conclusion, the SA matrix demonstrated its potential in protecting EOS probiotics during freeze-drying, from oxygen exposure, and during colonic administration. The findings from this study can serve as a reference for future applications in EOS probiotic encapsulation.

Mots-Clés: sodium algintae, next, generation probiotics, controlled release, oxygen barrier property.

*Intervenant

Membrane vesicles from Lacticaseibacillus casei BL23 enhance biofilm formation in a protein-dependent manner

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Résumé

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Membrane vesicles (MVs) are lipid nanostructures ranging from 20 and 400 nm in size, containing macromolecules such as proteins, nucleic acids and toxins. Initially regarded as mere cellular waste, bacterial MVs are now recognized for their role in host cell inflammatory response, communication between microorganisms or as a structure within biofilms.

Mainly studied in Gram-negative bacteria, MVs in Gram-positive bacteria also present interesting functions. Our laboratory recently demonstrated that *Lacticaseibacillus casei* BL23 MVs inhibit biofilm development in certain pathogenic and commensal bacteria (da Silva Barreira *et al.*, 2023). In addition, research has shown that MVs play a key role in biofilm formation in some bacterial species such as *Helicobacter pylori* by releasing extracellular DNA to help structure the biofilm, or *Streptococcus mutans* by supplying proteins that promote biofilm formation.

However, the role of MVs in biofilms formed by lactobacilli remains poorly understood. To better understand their function, we are studying the effect of MVs from mutants unable to synthesize the main proteins detected in *L. casei* BL23 MVs on interspecies biofilms.

MVs are obtained from culture supernatants concentrated by ultrafiltration and purified by ultracentrifugation. They are then characterized in terms of size and concentration before being inoculated into *L. casei* BL23 biofilm cultures. Biofilms are quantified using crystal violet and confocal microscopy techniques.

Our results show that the addition of MVs to biofilms appears to increase their biomass. In addition, BL23 mutants forming large biofilms produced MVs that were more beneficial to biofilm formation than MVs from the wild-type strain. The effect of promoting biofilm formation appears to be dose-dependent and possibly linked to the protein composition of the MVs.
These results suggest a role for *L. casei* BL23 MVs in biofilm formation, depending on their molecular composition. Understanding the mechanisms by which MVs influence biofilm development may open new routes for optimizing microbial communities or developing anti-biofilm strategies.

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Mots-Clés: Membrane vesicles, Biofilm, Lactobacilli