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HIGHLIGHT

1st CONGRESS OF THE SOCIEDADE DE CIÊNCIAS MÉDICAS DE LISBOA

Rethinking Medicine: Innovation, Collaboration, and the Health of the Future

PERSONALITIES: ONE LIFE IN MEDICINE
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EDUCATIONAL ARTICLE
Three Misconceptions in Medical Education: Student Evaluation of Teaching, Curricular Repetition, and Assessment Objectivity

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

EDITORIAL

Medicine and Technology: A Partnership Shaping the Future

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Medicine and technology have gone hand in hand for centuries. However, it was particularly in the last about 150 years that this development assumed truly impressive proportions. This was largely due to the widespread scientific and technological advances at the end of the 19th century in sequence of the so-called Industrial Revolution. This development influenced all areas of knowledge, including arts and humanities. In the field of medicine, this progress was driven, on the one hand, by unprecedented advances in biology and physiology and, on the other, by the discoveries in the fields of electricity, electromagnetic radiation, and radioactivity. Together, these factors enabled the emergence of innovative diagnostic and treatment tools, such as instrumentation for the acquisition of electrophysiological data, X-ray imaging, and, later, nuclear medicine as a whole. This symbiosis between medicine and technology expanded the limits of both.

The 20th century thus stood out as a period of extraordinary advances in diagnostic and data acquisition technologies. The introduction of digital technology, from the middle of the last century onwards, was crucial to the improvement and widespread use of existing analog technologies, as well as enabling the development of entirely new solutions. A significant milestone was the appearance of computed axial tomography (CAT) in the early 1970s — the first major success of digital technology and computing applied to medicine. Other notable advances followed, such as magnetic resonance imaging (MRI). These are just a few of the several examples demonstrating how the collaboration between medicine and engineering has resulted in stories of great success, especially in areas such as surgery — particularly neurosurgery —cardiology and pathological anatomy.

Thus, it can be said that the 20th century was essentially marked by the development of data acquisition technologies — imaging, laboratory, or physiological.

At the end of the 20th century and early 21st century, the paradigm began to change. The development of digital devices with high computational capacity, namely graphics processors (GPU), made it possible to improve and use processing algorithms that had begun to be developed in the 1970s and 1980s but which had no practical application due to a lack of available computing power.

> *Symbiosis between medicine and technology expanded the limits of both (…)*
>
> *For the first time, the role of data interpretation that was once exclusively reserved for doctors can now be shared with machines.*

Of this set of computing technologies, generally referred to as machine learning, deep learning algorithms stand out, as their functioning is inspired by the physiology of the brain. In recent years, it has become possible to implement algorithms for processing and analyzing the enormous variety of multimodal data that we are now able to generate easily and at low cost. For the first time, the role of data interpretation that was once exclusively reserved for doctors can now be shared with machines. It seems that computers have taken another qualitative leap forward and are now capable of performing high-level data analysis that was typically reserved for humans. What appears to be happening is that this process is only just beginning, and the remarkable results already achieved with Generative Artificial Intelligence are just the tip of the iceberg of what will be accomplished in the decades to come.

Therefore, it is clear that collaboration between doctors and engineers is here to stay and the two communities will have to work in an increasingly interconnected way. Doctors will have increasingly technological knowledge and engineers working on health applications will have increasingly greater knowledge of medicine. There has been talk for some time about training physicians-engineers. At the moment, the closest thing we have is biomedical engineers.

For these reasons, the Lisbon Society of Medical Sciences (SCML) has decided to create a Biomedical Engineering group, the aim of which is to propose initiatives that promote contact between these two communities that are so interdependent on each other. It is hoped that the launch of this latest issue will make a significant contribution to towards closer ties in favor of science and patients.

Doctors will have increasingly technological knowledge and engineers working on health applications will have increasingly greater knowledge of medicine

João Sanches
Member of the Editorial Board (JSCMed)

CHIEF EDITOR'S NOTE

With this issue, we gladly welcome the Universidade Católica de Lisboa - School of Medicine as a partner, endorsing the Journal of the Sociedade de Ciências Médicas de Lisboa (JSCML) as its official scientific publication.

From now on, our journal became the official scientific publication of the three schools of medicine in Lisbon.

We are strongly convinced that this partnership will be a fruitful tool in the development of health sciences in Portugal.

Victor Oliveira

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

ONE LIFE IN MEDICINE

António Gentil Martins

By
Victor Oliveira

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António Gentil da Silva Martins was born on the 10th of July 1930 and graduated in medicine from the Faculdade de Medicina – Universidade de Lisboa (Medical Faculty of the University of Lisbon). He early decided to pursue a career in pediatric surgery. His training included a scholarship in the United Kingdom, namely in London, at the Hospital for Sick Children (at Great Ormond Street), working under Sir Denis Browne and David Innes Williams. He later moved to Liverpool's Alder Hey Children's Hospital, working under Isabella Forshall and Peter Paul Rickham. In 1960, he started in Lisbon a medical-surgical pediatric unit for children, the first in the world. He was a founder of the International Associations for the Care of Children with Cancer (SIOP and IPSO) and became an honorary member of both. He pursued his medical career at the Lisbon pediatric hospital, the "Hospital Dona Estefânia", becoming head of the surgery department, and was also appointed as professor of pediatric surgery at "Nova Medical School" – Faculdade de Ciências Médicas de Lisboa. Furthermore, he practiced pediatric surgery in several areas, which gave him special skills when he dealt with conjoined twins. Dur-

António Gentil Martins at the Ordem dos Médicos' gallery of presidents, next to his own portrait.
(Photo: Victor Oliveira)

ing his long career, he operated on 7 pairs, with 9 children surviving, which was an outstanding achievement.

His commitment to medicine led him to fight for the rights and dignity of the medical profession, as well as for the patients' sake. He presided over the "Ordem dos Médicos,"[1] the Portuguese medical association, from 1977 until 1986, during a particularly agitated social and political period in Portugal. Following in his father's footsteps, he also successfully practiced several sports, especially shooting, having participated in the Olympic Games of Rome in 1960.

He is the heir to distinguished medical ancestry. His father, **António** Augusto da Silva **Martins** (1892/1930) was a surgeon who worked with the neurologist Egas Moniz, performing, under his supervision, the first cerebral angiogram. He invented an instrument (bearing his name) that allowed the clamping of the carotid artery, an essential step to the success of the procedure. António Martins was a multifaceted person also receiving recognition as a patriot, joining voluntarily, as a doctor, the Portuguese troops in the French trenches during the First World War. He was also a sportsman, practicing various sports in Portugal and abroad, taking part in the 1920 Olympic Games in Antwerp and the 1924 Olympic Games in Paris in the shooting discipline[2]. Unfortunately, his life was short, dying tragically in an accident with his rifle at a shooting range, in 1930[3]. His son, António, was not even 3 months old.

His grandfather, **Francisco** Soares Branco **Gentil** (1878-1964) was a professor of surgery who dedicated most of his life to fighting cancer. He

For over half a century, António Gentil Martins has been dedicated to pediatric surgery, performing extraordinary feats such as separating seven pairs of conjoined twins. However, his legacy extends beyond the operating room: he has been a steadfast advocate for medical ethics and a leader in the fight for the rights of patients and physicians in Portugal, leaving an indelible mark on global medicine."

founded a public hospital for the care of patients with cancer: the "Instituto Português de Oncologia" (Portuguese Oncology Institute), a prestigious Institution that still remains a pillar of cancer treatment in Portugal, with several branches spread throughout the country. He was also the medical advisor on the technical board for the construction in 1953 of the University Hospitals of Santa Maria (Lisboa) and S. João (Porto) and also the "Maternidade Alfredo da Costa," still the largest maternity in Lisbon. In the ancestry of António Gentil Martins figures Francisco **Soares Franco** (1771–1844)[4] a chairman of anatomy and director of the University Hospital in Coimbra. He was the first president of the scientific medical society: "Sociedade das Ciências Médicas de Lisboa," in 1822,[5] one of the oldest in the world.

António Gentil Martins keeps strong convictions both in medicine and sports, particularly in ethical domains. He is a strong defender of ethics in the medical profession, protecting both physicians and patients. He bears definite positions about sporting truth and is very critical of the gender reassignment of athletes based on their sexual characteristics. In his nineties, he still is an active participant in medical events, and his thoughts are very much taken into consideration.

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CONGRESSO
REPENSAR A MEDICINA:

Inovação, Colaboração e a Saúde do Futuro.

24 MAIO 2025

Medicina ULisboa
Campus de Torres Vedras
TORRES VEDRAS

SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

PRO INCOLUMITATE CIVIUM

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I CONGRESSO / 24 MAIO 2025

Medicina ULisboa
Campus de Torres Vedras
TORRES VEDRAS

RETHINKING MEDICINE: INNOVATION, COLLABORATION, AND THE HEALTH OF THE FUTURE

SCIENTIFIC PROGRAM:

The 1st Congress of the Sociedade das Ciências Médicas de Lisboa aimed to promote a debate on the importance of interdisciplinarity linking investigation and medical practice.

10h00-10h15 Abertura do Congresso
JOAQUIM FERREIRA, HUGO PINTO-MARQUES

10h15-11h15 Sessão Plenária I
A CONSULTA MÉDICA NO SÉCULO XXI: PILAR ESSENCIAL OU MODELO EM TRANSFORMAÇÃO?
MODERADOR: CATARINA LIMBERT

- **A Consulta Médica: Origem, Evolução e Perspectivas**
  PALESTRANTE: ANTÓNIO SOUSA GUERREIRO
- **A Tecnologia e a Consulta Médica: Complemento ou Substituto?**
  PALESTRANTE: PEDRO GOUVEIA
- **O Formato e Papel das Equipas Multidisciplinares**
  PALESTRANTE: ANA ABREU

11h15-11h30 COFEE BREAK

11h30-12h00 A Interdisciplinaridade como Pilar da Medicina Moderna
PALESTRANTE: MIGUEL SEABRA

12h00-13h00 Sessão Plenária II
ONE HEALTH: INTERDISCIPLINARIDADE E COLABORAÇÃO NA SAÚDE GLOBAL
MODERADOR: HUGO PINTO-MARQUES

- **One Health em Ação: Lições Aprendidas com a Pandemia a SARS-CoV-2**
  PALESTRANTE: FILIPE FROES
- **A interconexão Saúde Ambiente: o Impacto nas Alterações Ambientais**
  PALESTRANTE: JOÃO QUEIROZ E MELO
- **Como Construir Redes Colaborativas para Saúde Global?**
  PALESTRANTE: ANDRÉ PERALTA

13h00-14h00 ALMOÇO

14h00-14h30 Educação Interdisciplinar em Medicina: Preparando a Próxima Geração
PALESTRANTE: HELENA CANHÃO

14h30-15h30 Sessão plenária III
INVESTIGAÇÃO TRANSLACIONAL: INTEGRANDO CIÊNCIA, TECNOLOGIA E CUIDADOS PARA O FUTURO DA MEDICINA
MODERADOR: JOAQUIM FERREIRA

- **Da Descoberta à Cura: A Jornada Translacional**
  PALESTRANTE: MIGUEL PRUDÊNCIO
- **Como Aumentar a Probabilidade de Sucesso**
  PALESTRANTE: LUÍS ALMEIDA
- **Desafios Éticos e Regulatórios**
  PALESTRANTE: RUI NUNES

15:30-16:00 COFEE BREAK

16h00-17h00 Sessão Plenária IV
NOVOS MODELOS DE ESTUDOS CLÍNICOS: INOVAÇÕES, DESAFIOS E OPORTUNIDADES
MODERADOR: A VAZ CARNEIRO

- **Ensaios Clínicos Adaptativos: Flexibilidade e Eficiência**
  PALESTRANTE: JOAQUIM FERREIRA
- **O Uso de Big Data e Inteligência Artificial nos Estudos Clínicos**
  PALESTRANTE: ARLINDO OLIVEIRA
- **Real-World Evidence (RWE): A Utilização de Dados do Mundo Real**
  PALESTRANTE: TIAGO TAVEIRA GOMES

17:00 Encerramento

The Path Forward: Reflections from the 1st Congress of the Sociedade de Ciências Médicas de Lisboa

The 1st Congress of the Sociedade de Ciências Médicas de Lisboa (SCML), held on 24 May 2025 at the new Campus of the Lisbon School of Medicine in Torres Vedras, marked a strategic moment in the life of the Society.

Under the theme "Rethinking Medicine: Innovation, Collaboration and the Health of the Future," the congress brought together physicians, researchers, allied health professionals, and students in a space for critical, interdisciplinary, and open debate, promoting dialogue between clinical tradition, scientific innovation, and new models of healthcare organisation.

The scientific programme reflected this ambition. The opening session addressed the evolution of medical consultation, questioning whether this pillar of clinical practice is undergoing reformulation or is at risk of disappearance. The role of technology as a complement, or possible substitute, to face-to-face interaction was discussed, and a reorganisation of care centred on multidisciplinary and interdisciplinary teams, better suited to the complexity of patients and the diversity of health needs, was advocated.

Miguel Seabra's lecture reinforced the idea that interdisciplinarity is an essential condition for generating innovation with real impact.

The plenary session dedicated to the One Health concept highlighted how human health is deeply interconnected with animal and environmental health. Lessons from the SARS-CoV-2 pandemic were revisited, the environmental implications of healthcare were analysed, and strategies for building collaborative networks in global health were discussed.

Helena Canhão, head of Nova Medical School, discussed medical education, pointing towards more interdisciplinary curricular models adapted to the current and future realities of clinical practice.

The session on translational research emphasised the articulation between basic research, clinical research, and drug development, with concrete examples of biomedical innovation originating from academia. Strategies to increase efficiency in the development processes of new treatments and the ethical requirements that should guide all stages of research were also debated.

The final plenary session addressed new models of clinical studies, with concrete proposals to review how we develop and evaluate therapeutic innovation. Adaptive trials, the growing role of Big Data and Artificial Intelligence, and the use of Real-World Evidence (RWE) as an essential complement to traditional clinical trials were discussed.

This congress, in its inaugural edition, reaffirmed the founding mission of the SCML de Lisboa to foster dialogue between disciplines, promote medical science, and contribute to the advancement of medicine and society.

At a time when medicine faces unprecedented challenges, from the overload of healthcare systems to the demands of digital and demographic transition, it is imperative to create spaces for critical discussions and the construction of solutions. The success of this inaugural edition is proof that the SCML has the competence and vision to fulfil this role.

Joaquim J Ferreira

Vice-Dean of the Lisbon School of Medicine; President of the Sociedade de Ciências Médicas de Lisboa; Clinical Director of CNS - Campus Neurológico

EDUCATIONAL ARTICLE

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

Three Misconceptions in Medical Education: Student Evaluation of Teaching, Curricular Repetition, and Assessment Objectivity

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ABSTRACT: Three widely held assumptions in medical education may inadvertently hinder effective learning. First, student evaluations of teaching (SETs) are often treated as proxies for educational quality, yet they are shaped by factors unrelated to actual learning and provide limited actionable insight. Second, repetition in the curriculum is frequently dismissed as poor design rather than recognised as essential for mastery, reinforcing knowledge, developing fluency, and enabling long-term retention. Third, the overemphasis on objectivity in assessment, exemplified by multiple-choice questions (MCQs) and objective structured clinical examinations (OSCEs), may obscure important dimensions of clinical reasoning and are weak predictors of real-world clinical competence. Reconsidering these three assumptions may help realign educational strategies with their central goal: preparing students to become competent, reflective, and effective physicians.

KEY WORDS: Medical education, myths, repetition, student evaluation of teaching, objectivity

INTRODUCTION

The number three carries a powerful resonance in human cognition, education, and culture. It ranges from triads in diagnostic reasoning and vaccine schedules in medicine to the three-act structure in storytelling. The so-called "Rule of Three" (Latin: omne trium perfectum) reflects our preference for completeness, pattern recognition, and cognitive efficiency[1-3] and even in medical education, the power of three apparently has an effect [4]. In this spirit, three prevailing tenets of contemporary medical education merit critical re-examination: (i) the outsized role of students' evaluations of teaching; (ii) the drive to eliminate (curricular) repetition; and (iii) the overvalued ideal of objectivity in assessments.

1. Are students' evaluations of teaching (SETs) really that informative and relevant?

Do SETs, widely accepted and central to faculty appraisal systems, truly reflect educational quality, or are they merely popularity metrics? Despite their prominence, SETs are not strongly supported by current research [5]. A meta-analysis of over 100 different courses showed that students do not learn more from professors with higher SET since there is no significant correlation between SETs and actual learning [6], while a systematic review concluded that SETs are "questionable for high-stakes decisions," being heavily influenced by student bias and grade expectations [7]. In fact, a 2025 study across 160 veterinary courses found for the first time in veterinary medicine, a small but negative and statistically significant relationship between SET and an independent measure of learning [8]. Rather than reflecting educational value, SETs seem to mirror a broader trend toward instant ratings, reducing evaluations to a superficial popularity contest. While SETs may have limited utility, such as flagging an unprepared lecturer or unprofessional behaviour, they should be recognised for what they are: inherently subjective, often inconsistent, and frequently unrepresentative. They have little to do with what ultimately matters: whether students are learning and developing into competent physicians. Furthermore, it is at least unclear what the consequences are of a poor SET in terms of curriculum and education methodology changes, at least in medical schools.

2. In Praise of Repetition: Not a Design Flaw, but the Foundation of Mastery

The second misconception treats curricular repetition as a design fault rather than a pedagogical necessity. Students often describe repeated content as boring or redundant, an attitude perhaps intensified in today's mobile phone and social media generation, where novelty is constant, attention is fragmented, and initial enthusiasm fades quickly (novelty effect) [9]. In this mindset, long-term retention of knowledge is often sacrificed in the pursuit of the new. This perspective also feeds a deeper misconception: that medicine is about grasping complex concepts once (e.g. the Embden–Meyerhof pathway), and that once understood, repetition becomes unnecessary. While this may apply to isolated theories, most of medicine is different. It is more like learning a language, where progress depends on memorizing vast amounts of grammar and vocabulary, and fluency requires repeated reinforcement. If "appropriate antibiotic use" were a language, then its terminology and internal structure would need to be repeatedly driven deep, across pharmacology, microbiology, infectious diseases, and beyond, until students can speak it with fluency and precision.

Like in many areas of life, mastery in medicine rarely comes from novelty; it is built through repetition, feedback, and refinement. Rote memorisation, as used in language learning, is after all a form of repetition. While direct evidence on this is limited, studies consistently show that spaced repetition enhances learning and performance. Trials in microsurgical training, paediatrics rotations, and digital education all demonstrate that spaced repetition enhances knowledge, skills, and clinical outcomes [10-12]. A related idea is captured in Harden's spiral curriculum, which reinforces learning by systematically revisiting key topics at increasing levels of complexity [13]. A touch of novelty may still spark attention [14], but it is repetition that builds mastery.

3. Does our obsession with objectivity risk neglecting what really matters in assessment?

The third misconception is that only objective formats such as multiple-choice questions (MCQs) or objective structured clinical examinations (OSCEs) are the most valid ways to assess competence. This belief may be appealing, especially as it aims to address students' (often prioritized) demands for fairness and transparency. But it can also be misleading.

Curiously, nobody insists that a driving test be fully standardised or stripped of subjective judgement. While certain tasks, like parallel parking or emergency stops, are standardised, we ultimately care whether the driver in the next lane can actually drive, not just whether they passed a checklist of manoeuvres. That judgement depends on the examiner's expert ability to assess how well a person integrates knowledge and skills in real situations, something oral examinations in medicine are uniquely suited to capture. In contrast, this is difficult to assess in OSCEs, if not overlooked entirely, where assessment is fragmented into narrowly scripted tasks and scored against rigid checklists.

Standardization has a role in ensuring fairness, comparability, and clarity. Although OSCEs were a well-intentioned attempt to address inconsistencies in traditional assessments, over-reliance on their rigid format can limit what we are able to assess. They should be part of a broader assessment strategy, not the sole

measure, just as a driving examiner uses a checklist alongside real-time observation and judgement. A 2023 systematic review found structured oral exams (vivas) to be both reliable and well-accepted [15]. Meanwhile, a scoping review of OSCEs found that in 78% of studies, they correlated only weakly with written tests and real-world performance, particularly with poorly trained examiners [16]. Instead of overemphasising standardisation in the name of objectivity, should we not be asking the more important question: does the assessment, even at the cost of some subjectivity, help us judge whether a student is becoming a competent physician?

CONCLUSION

Modern educational practices often promise progress, but their impact on the real goal, producing competent physicians, is often uncertain. Some rest more on assumption than evidence, and not everything old is obsolete, especially if it worked. Student evaluations often reflect popularity more than learning, repetition remains the foundation of mastery, and rigid objectivity may obscure true competence. Ultimately, what matters is that our teaching and assessments truly help students become good doctors, equipped to deliver high-quality, patient-centred care.

DISCLOSURES: *The views and reflections expressed in this article are solely those of the authors and do not necessarily represent the official position of the School of Medicine with which they are affiliated.*
The authors used artificial intelligence (AI) tools – including GPT-4, Google Gemini, and DeepSeek (version/date of use: May 2025) – exclusively for language editing and clarity enhancement. No AI-generated content was used for original analysis, interpretation, or development of arguments. AI support was limited to grammar and stylistic refinement at the sentence level and did not involve the generation of original or substantive content.
No identifiable or sensitive data were shared with GPT-4, Google Gemini, or DeepSeek during the editing process. All usage complied with institutional privacy and security guidelines. The final manuscript was reviewed and approved by all authors to ensure accuracy and adherence to ethical standards for research and publication.

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Health Communication in Portugal: Current Challenges and Prospects

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ABSTRACT: Background: Health communication is a fundamental component of public health promotion and is crucial for disseminating information, raising public awareness of healthy behaviours and managing health crises. In Portugal, health communication has evolved over the last few decades, adapting to new technologies and the growing need for accurate and accessible information. However, there are still significant challenges that impact its effectiveness, such as inequitable access, pervasive misinformation and over-reliance on digital platforms. **Aim:** This narrative review critically examines the current challenges shaping health communication in Portugal, identifies progression and limitations within existing practice, and proposes evidence-informed priorities for Health Communication in Portugal through current Challenges and Prospects' improvement, grounded in recent data and emerging trends. **Methods:** A qualitative narrative analysis of peer-reviewed literature and policy documents, published between 2010 and 2025, was embraced. **Results:** Persistent barriers include social and digital inequities, misinformation and variable institutional capacity. However, health-literacy initiatives and data-driven campaigns show measurable progress. **Conclusions:** Tackling these barriers will require coordinated, inclusive and technologically enabled strategies that strengthen trust, promote equity and optimize health outcomes in Portugal.

KEY WORDS: Health communication; health literacy; health promotion; disease prevention; population

INTRODUCTION

Historically speaking, health communication relied on transmissive, vertical models, centred on the dissemination of messages by the state, aimed at changing individual behaviour.[1-4] Over time, these models have been replaced by more participatory, dialogic, citizen-centred approaches that recognize the active role of individuals in managing their health.[1,3,4]

Until the end of the 20th century, health communication in Portugal was dominated by awareness-raising campaigns promoted by health authorities, with

an emphasis on normative messages, often centred on individual responsibility.[4] Vaccination, smoking cessation, hygiene and family planning campaigns were mainly publicized through traditional media – television, radio and the press – structures which were poorly adapted to different audiences.[1-4] This top-down approach proved limited, particularly in contexts of low health literacy and socio-economic inequalities, hindering information assimilation.

Health communication is an essential tool for promoting public health, preventing disease and improving the population's health literacy.[1] In Portugal, the field has evolved alongside technological, social and political change. From mass-media campaigns to today's digital and AI-enabled tools, health communication has become a strategic and transversal area, especially in crisis contexts, as demonstrated by the COVID-19 pandemic.[1-4]

Nevertheless, limited information access, low literacy levels and regional inequalities continued to constrain effective communication. Portugal is now experiencing a transformation in health communication: the culture within the field has become more strategic, multidirectional, segmented and adapted.[5,6] Social networks, digital platforms, influencers and mobile technology have reshaped these dynamics.[5,6] The Directorate-General for Health [DGS] and the National Health Service [SNS] increasingly leverage digital channels, data and algorithms to personalize campaigns, issue health alerts and monitor impact, positioning health literacy as a strategic priority.[7,8]

Caregivers, volunteers, health influencers, local communities and associations will play a crucial role in fostering culturally and linguistically sensitive, proximity-based communication that promotes citizen autonomy.[7,9,10] The COVID-19 pandemic underscored the need for clear, empathetic, evidence-based messaging, tailored to diverse audiences while exposing the corrosive impact of misinformation on trust and compliance.[11,12]

Emerging technologies – including AI, big data, chatbots, augmented reality and interactive platforms – will be strategies that will continuously shape Portuguese health communication; however, empathy, active listening and accessibility must remain key procedures too.[13] Public policies that promote inclusion, clarity and transparency in citizen communication will be therefore essential.[13] In sum, health communication serves as a strategic pillar of public health policy, influencing behaviour, advancing literacy and strengthening institutional trust.[14]

Interest in the field has surged in recent decades as new communication formats emerge and citizen participation gains prominence.[13,15,16] Health communication can be understood as a process of sharing information with the aim of improving health and general well-being. It involves multiple actors – health professionals, managers, the media, public institutions and civil society – institutions and individuals that employ diverse strategies to achieve this goal.[1,4,6,12] Health communication plays a fundamental role in health promotion, disease prevention and improving health literacy.[2,7,10,17] Health literacy is defined as the ability to access, understand, evaluate and use information to make health decisions: A key concept in health communication.[2,17]

As an inherently interdisciplinary field, health communication synthesizes insights from communication science, public health, medicine, psychology, sociology, economics, political science, data science and emergent domains such as health informatics and entomology.[15,18,19]

Accordingly, this narrative review analyses the historical evolution of health communication in Portugal, identifies persistent barriers and recent advances, and outlines future priorities – particularly the integration of artificial intelligence and user-centred strategies – to enhance equity and effectiveness.

METHODS

This article adopts a qualitative and exploratory narrative review approach, based on a bibliographic and documentary review of national and international sources, including scientific literature, reports from the Directorate-General for Health [DGS], and documents from the World Health Organization [WHO].

The research searched scientific sources indexed in PubMed, B-on, Web of Science and Scopus, covering the last 15 years (2010-2025) with the aim of critically analysing the historical evolution, contemporary challenges and future prospects of health communication in Portugal. The core Boolean string – "health communication" AND "Portugal" AND ("literacy" OR "promotio"n OR "digita"l) – was adapted to each database.

A narrative review was chosen because it allows for an interpretative, comprehensive and flexible approach, which is particularly suitable for complex, inter-

disciplinary and rapidly evolving areas of knowledge, such as health communication.

Data collection took place in the first few months of 2025 and included two main strands:

a) Systematised bibliographic search in international scientific databases;

b) Documentary analysis of institutional sources and national and international public policies.

Duplicate papers, purely clinical studies unrelated to communication and publications without peer review were excluded. Additional exclusion criteria included: (i) grey literature lacking verifiable authorship, and (ii) articles not available in Portuguese or English.

After identifying and selecting the sources, the documents were subjected to initial skim The National Health Literacy Plan and subsequent analytical reading, using an inductive thematic analysis. Screening counts for each review stage (identification, de-duplication, title/abstract screening and full-text eligibility) were recorded, and the Mixed-Methods Appraisal Tool was applied to assess methodological quality[20]. This process enabled the identification of emerging categories related to the object of study. Triangulation between scientific sources and institutional documents ensured credibility and interpretative consistency, allowing for a comprehensive and contextualized understanding of the phenomenon. As this is a narrative review with no involvement of human beings or primary data collection, no ethics committee approval was required. However, all the sources used were duly cited and respected the principles of academic integrity.

RESULTS

Improving health communication strategies has become a prioritized goal, especially in light of recent health crises, such as the COVID-19 pandemic, and in a scenario marked by increasing levels of misinformation surrounding health issues. This goal is directly linked to the sustained promotion of health literacy, a key factor in empowering citizens to make informed decisions and adopt healthier behaviours.[21–23] The development of effective strategies to improve health literacy at all levels of society is therefore crucial to achieving public health promotion goals. The creation and implementation of digital strategies reinforces the need for targeted interventions tailored to different segments of the population.[23–25]

Historical patterns (1900s – 1990s): For much of the 20th century, health communication in Portugal followed an informative, unidirectional model, based on technical authority and mass media. Vaccination, public hygiene and smoking-prevention campaigns mainly used television, radio and posters.[5] Because health literacy was low and access to information unequal, these campaigns achieved only modest reach and impact.

Shift to participatory, data-driven strategies (2000s – present): In recent decades, there has been a shift towards more interactive, segmented and data-driven strategies.[7,9] Key milestones include the National Health Literacy Plan and the DGS Health Communication Strategy, institutions that introduced a new logic, based on empowering citizens and using communication as a tool for behaviour change.[7,9] Portugal has thus made significant progress in modernizing health communication, promoting a transition from vertical models to citizen-centred approaches rooted in health literacy.[13] The application of the potential of transmedia narratives as innovative and effective tools for strengthening health literacy, not only in Portugal but also in international contexts, has contributed to a more informed, participatory and autonomous citizenry in health matters, as well as enabling more efficient management of health system resources at the national level.[21–23]

Persistent barriers and emerging opportunities: Despite progress, the future will require a balanced approach between technological innovation and human values, with investment in training professionals, to lead the cause in fighting disinformation and strengthening citizen participation.[13] Health communication is not just a technical tool, but a social, relational and strategic practice that requires dialogue, trust and a commitment to equity. However, social networks and digital platforms, while increasingly prominent, continue to mirror inequalities in access and carry risks associated with misinformation. At the same time, artificial intelligence and personalization offer growing potential to tailor messages and monitor their impact.[8,18,26]

The application of the potential of transmedia narratives as innovative and effective tools for strengthening health literacy, not only in Portugal but also in international contexts, contributes to a more informed, participatory and autonomous citizenry in health matters, as well as enabling more efficient management of health system resources at the national level.[27] Health literacy has taken on a central role in the

analysis of health systems, especially in understanding how individuals interact with the various components of these systems. Health literacy levels directly influence the ability to make appropriate health decisions, with a direct impact on individual and familiar quality of life. This reality is particularly relevant in a demographic context such as Portugal's, a country marked by an ageing population and an increased number of dependent people, whether that is through younger or elderly demographics.

Low levels of health literacy are often associated with a reduced ability to manage chronic diseases, difficulties in resolving situations that could be treated at home, a higher rate of avoidable hospitalisations, excessive use of emergency services and lower adherence to preventive practices. Health literacy should therefore be seen as a strategic priority, with direct effects on the sustainability and efficiency of health systems. [8,21–25,27]

DISCUSSION

The results show that health communication in Portugal still faces several major obstacles, yet the findings also reveal clear opportunities for enhancement. The integration of new technologies into health communication presents both challenges and advantages. On one hand, digitalization facilitates access to information and allows public health campaigns to reach a wider audience. On the other hand, it can entrench disinformation and digital exclusion if it is not well regulated. Personalized communication, through digital platforms and telemedicine, has the potential to further empower the population, especially in the management of chronic diseases. However, the adaptation of health professionals to these new forms of communication is still an ongoing process, and the lack of adequate training can jeopardize relationships with the population. During the COVID-19 pandemic, the importance of clear, empathetic and transparent risk communication was emphasized, reinforcing the role of social media and official digital channels, but it simultaneously exposed the speed and scale of infodemics. Persistent challenges therefore include curbing misinformation, tailoring language to diverse literacy levels and embedding systematic communication training into health curricula. Looking ahead, big data, artificial intelligence and chatbots, can optimize the delivery of messages based on user behaviours and profiles, provided their algorithms remain transparent and equity-oriented.

However, these innovations require ethical and privacy assurances, digital inclusion to avoid inequalities and integration with humanized communication practices centred on empathy and active listening. Continuous training in communication and digital skills for health professionals and the promotion of critical citizenship will be fundamental to guaranteeing effective and inclusive communication. Portugal's trajectory – from top-down broadcasts to interactive, citizen-centred dialogue – demonstrates tangible progress but also reveals remaining gaps. It is now recognized as a fundamental tool for health promotion and disease prevention, with the potential to transform the way society relates to health. Going forward, technology and humanism must be integrated so that communication remains efficient, inclusive and ethically grounded. Health communication can help reduce health inequalities however it may also widen them if the sources of disparity – access, exposure and behaviour change barriers – are not addressed. Investing in participatory strategies, strengthening health literacy and empowering professionals and citizens to communicate more consciously and critically are essential steps towards a more resilient, fair and people-centred health system.

Improving public health communication during a global crisis is essential to strengthening community resilience. The COVID-19 pandemic has clearly highlighted the central role of public health in defining effective strategies and making intelligent use of digital tools to combat the infodemic and disseminate reliable information. To tackle future epidemics, it is essential that health professionals develop and improve their communication skills, in order to strengthen public confidence and promote protective behaviors.[27]

At the same time, social media and other digital platforms play a strategic role in managing communication in emergency situations. They should therefore be studied, understood and used critically and effectively as channels for outreach, mobilisation and health literacy. Digital social networks, such as Facebook, are becoming increasingly relevant platforms for health communication, offering wider information dynamics than traditional media. These tools bring patients and health professionals closer together, reinforce therapeutic adherence, promote health literacy and offer emotional and social support to individuals.[27]

There is still a lack of studies that systematically analyse the role of negativity and positivity in communication about diseases, especially in digital contexts.

The construction of health messages can be analysed at two fundamental levels: micro and macro. On one hand, the micro level, given that this is where emotional appeals and the theoretical structure of the message, strongly associated with positive or negative valence, fit in. On the other hand, the macro level includes strategies based on behavioural theories, responsible for designing messages aimed at promoting behavioural change in health.[25]

CONCLUSION

Health communication in Portugal must balance technological innovation with ethical and humanistic principles. Investments in health literacy, training professionals and combating disinformation are fundamental to strengthen trust and improvement in health outcomes. Emerging tools – artificial intelligence [AI], chatbots, interactive platforms and predictive analytics – can design highly personalised strategies that reach specific groups according to risk profiles, habits and needs, provided that privacy tools and transparency are guaranteed. However, technology alone is insufficient; communication must continue to value the human element, fostering relationships of trust, active listening and empathy. Training in communication skills and investing in health education in schools and communities will be key to a more equitable and informed future. Health communication in Portugal faces considerable challenges, including misinformation, unequal access to information and message fragmentation, but also offers opportunities for transformation through cross-sector collaboration and citizen participation. A multi-sectoral strategy that prioritizes transparency, accessibility and personalisation can narrow information gaps and strengthen the health system as a whole. If well implemented, such changes could significantly impact and consequently, improve public health, reduce inequalities and add reinforcement in systemic resilience.

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Student Experiences in Third-year Hospital Internship Using Logbook Records

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ABSTRACT: Objective: This study aimed to evaluate whether third-year medical students' clinical internship met educational objectives and to assess students' perceptions of their clinical experience. **Methods:** A mixed-methods, descriptive, observational study was conducted with third-year medical students at Lisbon School of Medicine. Students logged their clinical activities using a digital logbook and completed a survey assessing their satisfaction with their supervisor and respective department, skills development, and overall experience. Descriptive statistics were used for quantitative analysis, while qualitative feedback was thematically categorized. **Results:** Of the 369 participating students, 99.5% completed the digital logbook, documenting their clinical activities. The data revealed strong engagement in core clinical procedures, with **cardiovascular, pulmonary, and abdominal examinations performed by over 85% of students.** In contrast, exposure to the **neurological, musculoskeletal, and genital-urinary systems was significantly lower, ranging from 26% to 64%.** Participation in key procedural and communication skills varied significantly, with **participation in writing patient charts by 54% and communication of bad news recorded by only 25% of students.** While survey responses indicated **high satisfaction** with the overall learning experience, variations in specialty exposure and procedural opportunities emerged as areas for improvement. **Significance:** Students demonstrated strong engagement in core clinical procedures and reported high satisfaction, but gaps in training for specific systems, communication skills, and hands-on training were identified. Addressing these disparities can enhance clinical education and improve alignment with curricular objectives.

KEY WORDS: Medical education, clinical rotation, student experience, digital logbook, curriculum alignment.

INTRODUCTION

Medical education requires the ability to integrate theoretical knowledge with clinical practice, yet the transition from classroom learning to bedside training presents challenges for both students and educators[1, 2]. To bridge this gap, it is essential that the medical curriculum continuously evolves, incorporating diverse teaching strategies that enhance clinical reasoning and procedural skills, but also promote student autonomy and provide constructive feedback and emotional support[3, 4]. These elements are closely tied to student motivation. When a student recognizes the practical relevance of their learning activities and feel confident in their ability to complete them, they are more likely to excel academically and clinically[4].

Clinical rotations play a pivotal role in medical training, as they offer an opportunity to cultivate this motivation, by allowing students to practice their skills and make important decisions in real-patient scenarios[5, 6]. However, when students are assigned to various hospitals under the supervision of different tutors, it can be challenging to ensure they receive consistent learning opportunities to develop these essential skills, an issue which has also been described by Schick et al. regarding the final year of undergraduate medical education in Germany[7].

To assess whether all students meet the core curriculum's clinical objectives, it is essential to document their learning activities systematically[8]. The use of logbooks becomes particularly useful in this setting, as they allow for supervision and monitoring of students' clinical work and for supervisor feedback, contributing overall to improving medical teaching[9, 10].

This study aims[1] to analyse students' first clinical experience and assess whether it aligns with the educational objectives set by the curriculum, and[2] to evaluate students' overall perception of their hospital rotation experience.

METHODS

Study Design

This study is a mixed-methods, descriptive, observational study incorporating prospective data collection and survey elements.

Educational Context and Curriculum Overview

Lisbon School of Medicine's 6-year master's program covers three years of theory (physiology, anatomy, pathophysiology) and three years of clinical rotations for hands-on experience.[11]

The course "Introduction to Clinical Practice" during third year consists of theoretical and practical classes, where students learn the basics of history taking and physical examination. This course is finished with a four-week clinical rotation intended as a bridge between pre-clinical and clinical training. This internship allows students to practice essential clinical competencies, while gaining practical experience with basic procedures, such as venous and arterial blood punctures.

Students are placed in various hospital departments under different supervisors, primarily around Lisbon. Supervisors are medical doctors with a financial connection to FMUL but are not necessarily part of the academic career. They are invited to an optional online meeting to clarify the goals and details of the clinical rotation, with the same information also provided by email. The clinical internship's primary goal is the completion of three individual case histories up to the initial diagnostic hypotheses, guided and evaluated by the tutor. Secondary objectives include integrating students into hospital practice, fostering teamwork, professional interactions, and patient-centred care. Students are expected to go beyond passive observation by actively participating in clinical activities under supervision. This includes history-taking and physical examinations, and accompanying tutors in emergency care, consultations, ward rounds, and clinical meetings.

Participants

The participants in this study were 369 third-year medical students from FMUL who were undertaking their clinical internships at various hospitals, primarily in the Lisbon region, during the 2023–2024 academic year. A detailed list of these hospitals can be found in Appendix A. Each student was assigned to a specific hospital department and to a supervisor for the four-week duration of their internship. This internship represented their first clinical rotation, providing an initial hands-on experience in medical practice. Additionally, students were using the Logbook App (Xerpa®) for the first time, integrating it into their workflow to document activities and monitor progress.

Data Collection

Data was collected using a mobile application

(Xerpa®), which served as a digital logbook (Appendix B) for students to document their daily clinical experiences. Filling out the logbook was mandatory, but non-compliance did not impact on students' evaluation. At the end of each day, students recorded the following information:

- **Core Clinical Procedures:** Students logged specific clinical tasks they performed, such as history taking, physical examinations, and basic procedures (e.g., venous and arterial punctures).
- **Frequency of Procedures:** Every time a student performed a clinical procedure, they were required to log it in the app, enabling the calculation of an average per student.
- **Additional Procedures (Free Text):** Students could document any additional procedures or clinical activities they observed or performed, using free text for unstructured input.

The app's data provided both quantitative information (frequency of core procedures) and qualitative insights (free-text entries and supervisor feedback).

At the internship's end, students completed an online survey (Appendix C) assessing:

- **Supervisor Engagement:** Support and guidance received.
- **Skill Development:** Opportunities to practice clinical procedures.
- **Recommendation Likelihood:** Willingness to recommend supervisor, department, and hospital.
- **Integration & Learning Satisfaction:** Ratings on team integration, learning quality, and digital logbook use (Likert scale 1–5).

Data Categorization

Data from the digital logbook was organized in Excel, grouping 72 Core Clinical Procedures by specialty. Free-text entries were categorized (e.g., surgeries, teaching sessions) to standardize varied descriptions. Survey feedback was also themed into positive (mentorship, learning) and negative (lack of support, limited practice) categories. For a detailed breakdown of this process, consult appendix D.

Data Analysis

The analysis was divided into quantitative and qualitative components:

Quantitative Analysis:

- **Descriptive Statistics:** Frequencies and averages were calculated for each core clinical procedure to assess common activities and exposure levels. Students' final grades were also analysed statistically. In Portugal, we use a 0-20 grading scale, being 0 equivalent to 0% and 20 equivalent to 100%.

Qualitative Analysis:

- **Analysis of Additional Procedures:** Free-text entries on additional procedures were grouped into predefined categories based on recurring themes to identify clinical tasks outside the core curriculum.
- **Survey Response Analysis:** Structured responses to the survey questions were analysed to calculate the frequency of answers (e.g. "Yes", "No", "Maybe").
- **Feedback Analysis:** Positive and negative feedback was categorized to highlight recurring themes, with multi-category responses included in all relevant themes.

Ethical Considerations

Informed consent was electronically obtained when the students logged in the app and answered the survey. All identifiers were removed by the app as the data was exported to Excel.

RESULTS

1. Clinical Activities Logged by Students

A total of 367 students (99.5% of the total) reported their clinical activities performed during the clinical rotation in the digital logbook. Table 1 presents the detailed breakdown of activities within each category. The most frequent tasks included **hand hygiene (10 times/student; 80% of all students)** and **taking complete clinical histories (5 times/student)**, with over 95% participation in history-taking. Skills like **cardiac auscultation (6 times/student)** and **pulmonary auscultation (6 times/student)** were widely practiced, with over 85% student involvement. **Writing patients charts (4 times/student)** was only registered by about half of the students (54%). Participation in more complex or specialized procedures, such as **arterial blood gas assessments (3 times/student)** and **digital rectal examinations (3 times/student)**, was less frequent, with less than 50% participation. Overall, task frequency and participation varied significantly across systems and

TABLE 1. Overview of core clinical activities logged by students

Physical examinations and Procedures	Number of Students	Percentage of all students (%)	Total of Performed Procedures	Average Frequency per Student
GENERAL TASKS				
Hand hygiene	293	79.84	3044	10
Hand desinfection technique	249	67.85	2102	8
Taking complete clinical history	352	95.91	1808	5
Discussion of main clinical diagnostic hypothesis	335	91.28	1789	5
Discussion of differential diagnosis based on clinical findings	315	85.83	1493	5
Patient rounds	259	70.57	1439	6
Participation in writing of patient charts	199	54.22	799	4
Participation in selecting additional diagnostic resources based on clinical findings	190	51.77	670	4
Obtain informed consent (oral/written)	159	43.32	540	3
Participation in Interview of patient family members	100	27.25	265	3
Participation in bad news transmission	91	24.80	176	2
CARDIOVASCULAR SYSTEM				
Cardiac auscultation	330	89.92	2069	6
Evaluation of arterial pulses	314	85.56	1189	4
Assessment of blood pressure	258	70.30	1033	4
Assessment of peripheral perfusion signs	255	69.48	803	3
Assessment of lymph nodes	259	70.57	770	3
Evaluation of cardiac thrill	156	42.51	432	3
Evaluation and interpretation of apical impulse	145	39.51	363	3
THORAX AND LUNGS				
Lung auscultation	312	85.01	1742	6
Inspection of thorax	302	82.29	1236	4
Assessment of respiratory rate	300	81.74	1160	4
Assessment of breathing pattern	253	68.94	917	4
Assessment of difficulty breathing signs	196	53.41	613	3
Percussion of anterior, posterior and lateral thoracic walls	215	58.58	542	3
Assessment of chest expansion	191	52.04	499	3
Assessment of tactile fremitus	155	42.23	372	2
Per-oral auscultation	66	17.98	140	2
Auscultation transmitted voice sounds	62	16.89	135	2
NERVOUS SYSTEM				
Evaluation of higher cognitive functions	235	64.03	754	3
Assessment of cranial nerves III, IV, VI	239	65.12	668	3
Assessment of cranial nerve VII	224	61.04	631	3
Assessment of muscular strength - general strength	207	56.40	583	3
Assessment of muscular strength - segmental strength	202	55.04	562	3
Assessment of cranial nerve II	213	58.04	560	3
Assessment of cranial nerve V	210	57.22	554	3
Assessment of cranial nerve XII	194	52.86	508	3
Assessment of muscular tonus	182	49.59	497	3
Assessment of sensitivity	182	49.59	461	3
Assessment of vestibulocerebellar function	178	48.50	432	2
Assessment of cranial nerve XI	175	47.68	428	2
Assessment of cranial nerve IX and X	163	44.41	410	3
Assessment of cranial nerve VIII	160	43.60	387	2

TABLE 1. *(continue)*

Physical examinations and Procedures	Number of Students	Percentage of all students (%)	Total of Performed Procedures	Average Frequency per Student
NERVOUS SYSTEM				
Assessment of deep tendon reflexes	133	36.24	334	3
Evaluation of meningeal signs	138	37.60	302	2
Evaluation of lasègue's sign	133	36.24	297	2
Assessment of cutaneous reflexes	103	28.07	229	2
Evaluation of Babinski sign	109	29.70	221	2
ABDOMEN				
Inspection of abdomen	312	85.01	1448	5
Palpation of abdomen	302	82.29	1248	4
Percussion of abdomen	289	78.75	1083	4
Auscultation of bowel sounds	292	79.56	1079	4
Assessment of irritation peritoneal signs	202	55.04	615	3
Evaluation of fluid wave sign	176	47.96	419	2
Evaluation of renal Murphy sign	106	28.88	195	2
MUSKULOSKELETAL SYSTEM				
Assessment of wrist and hand joints	153	41.69	492	3
Gate assessment	173	47.14	417	2
Assessment of knee joint	140	38.15	398	3
Assessment of elbow joint	140	38.15	378	3
Assessment of ankle joint and foot	131	35.69	378	3
Assessment of shoulder joint	136	37.06	375	3
Assessment of spine	141	38.42	334	2
Assessment of hip joint	113	30.79	305	3
Assessment of sacroiliac joints	104	28.34	268	3
GENITAL - URINARY SYSTEMS				
Inspection and palpation of the breast	95	25.89	216	2
Inspection of perianal area and digital rectal examination	29	7.90	84	3
HEAD				
Assessment of oropharynx	175	47.68	460	3
Palpation of perinasal sinuses	161	43.87	333	2
Inspection of the nose and nasal fossae	143	38.96	309	2
Inspection and palpation of the ear and otoscopy	99	26.98	225	2
PROCEDURES				
Interpretation of patient radiographs	217	59.13	751	3
Recording and interpretation of ECG	161	43.87	475	3
Arterial blood gas collection	131	35.69	361	3

procedures.

Table 2 contains the categorized activities students engaged in outside of the core curriculum, reported as free-text entries.

Students participated in various activities outside the core curriculum, with **45% observing or practicing specialty-specific techniques/procedures (2 times/student)** and 32% observing surgeries (1 time/student). Other notable activities included "**ambulatory consult observations" (6%, 3 times/student)** and "**physical examinations outside the core curriculum" (11%, 2 times/student).** This last category titled "Physical Examinations Outside the Core Curriculum" was created to encompass a variety of assessments that were not explicit in the logbook, such as "Evaluation of Pemberton Sign" and "Palpation of the Thyroid Gland." Less frequent activities included **minor surgeries (3%, 2 times/student), and participation in surgeries (3%, 1 time/student).**

2. The Online Survey

A total of 225 students (61% from total) responded to the final online survey, with key findings summarized in Table 3. The majority **felt supported by their supervisor** during clinical history-taking (89%) and **would recommend their hospital** (91%) **or department** (86%) to colleagues, but 26% reported spending more than half of their rotation with another doctor besides their supervisor. Additionally, 56% had opportunities to train procedures, but fewer (28%) were able to share clinical information directly with patients or relatives. These results highlight both positive aspects and areas for improvement in the internship experience.

The highest satisfaction was with **welcome, friendliness, and integration (mean 4.6, SD 0.7) – Table 4.** Learning opportunities and clinical skills training were also well-rated, with a **mean score of 4.3 (SD 1.0).** However, satisfaction with the **Xerpa App and logbook** was lower, with a **mean score of 3.4 (SD 1.1)**, indicating potential areas for improvement in the digital tools provided for the rotation.

Positive and negative feedback were analysed and are illustrated in Fig. 1 and Fig. 2, respectively. A total of 127 (35% of total) students provided positive feedback, with 52% highlighting an 'Enriching Learning Experience' as the most significant aspect of their rotation, followed by 24% who emphasized a 'Collaborative Team Environment.' Conversely, 84 students (23% of total) reported negative experiences, with the most frequently cited issues being 'Skill Development Gaps' (37%) and 'Limited Clinical Variety' (17%). Regarding the Xerpa app, some negative comments were found that might explain the lower satisfaction (supplement IV).

3. Student's Final Grades

The **mean and median of students grades** for the clinical rotation was 19, revealing that the students con-

TABLE 2. Activities outside the core curriculum logged by students

Activities outside the core curriculum	Number of Students	Total of performed procedures	Average Frequency per student	Percentage of all students (%)
Observation/Practicing of techniques/procedures specific to specialty	166	298	2	45
Observation of surgeries	118	169	1	32
Physical examinations outside core curriculum	39	97	2	11
Observation of ambulatory consults	21	62	3	6
Observation/participation in clinical teaching session	20	23	1	5
Minor Surgery	12	28	2	3
Observation of emergency room shifts	12	31	3	3
Participation in surgeries	11	15	1	3
Venous punctures	9	24	3	2
Assessment of peripheral edema	9	44	5	2
Observation of department meetings	8	29	4	2
Observation of MDT meetings	5	10	2	1

TABLE 3. Survey responses on student experiences and supervisor support

Questions	Yes	No	Maybe	Not answered
Other than your supervisor, were you with another doctor more than 50% of the rotation?	59 (26%)	164 (73%)	2 (1%)	0
Did you feel supported by your supervisor when taking Clinical Histories?	201 (89%)	16 (7%)	8 (4%)	0
Did you have the opportunity to train procedures (venous and arterial blood punctures, etc)?	127 (56%)	87 (39%)	9 (4%)	2 (<1%)
Did you have the opportunity to share clinical information with patients and relatives yourself?	62 (28%)	151 (67%)	11 (5%)	1 (<1%)
Were you asked to write patient clinical journals?	61 (27%)	157 (70%)	6 (3%)	1 (<1%
Would you recommend your supervisor to your colleagues?	186 (83%)	13 (6%)	25 (11%)	1 (<1%
Would you recommend you department to your colleagues?	194 (86%)	16 (7%)	14 (6%)	1 (<1%
Would you recommend the hospital to your colleagues?	204 (91%)	7 (3%)	13 (6%)	1 (<1%

TABLE 4. Mean satisfaction scores, standard deviations, and interpretations of clinical rotation experience

Questions	Mean Score	Standard Deviation
On a scale of 1 to 5, how satisfied are you with the welcome, friendliness, and integration in the department?	4.6	0.7
On a scale of 1 to 5, how satisfied are you with the learning opportunities and training in clinical skills?	4.3	1.0
On a scale of 1 to 5, how satisfied are you with the Xerpa App and logbook for this clinical rotation?	3.4	1.1

NOTE: Ratings were measured on a Likert scale from 1 ("Very dissatisfied") to 5 ("Very satisfied").

FIGURE 1. Distribution of positive feedback themes provided by students, shown as percentages

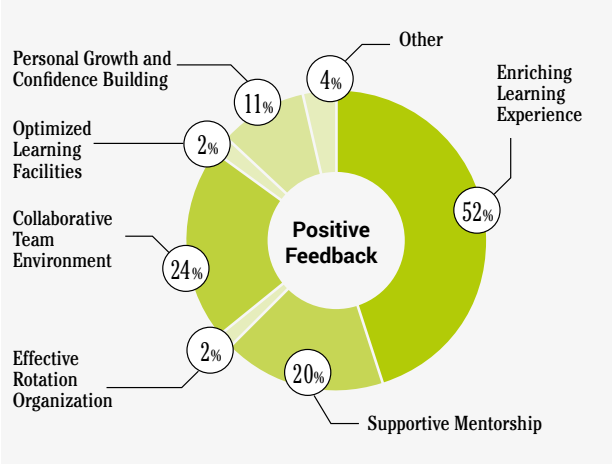
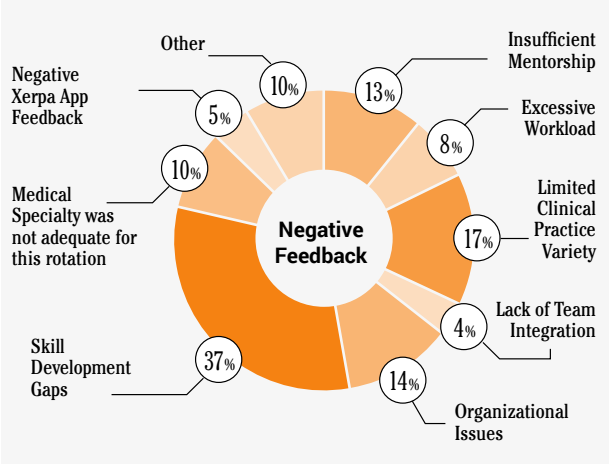


FIGURE 2. Distribution of negative feedback themes provided by students, shown as percentages



sistently obtained high grades in their rotations.

DISCUSSION

This study aimed to evaluate the first clinical experience of 3rd-year medical students and assess whether it aligns with the educational objectives set by the curriculum, as recorded in their digital logbook. Specifically, we assessed whether students' clinical training across diverse hospitals and supervisors provided consistent learning experiences that met the expected competencies. Additionally, the study sought to evaluate students' overall perception of their hospital rotation

experience, including levels of satisfaction, engagement in core clinical tasks, and perceived challenges.

Our findings highlight strong engagement in core clinical procedures, such as cardiovascular, pulmonary and abdominal examinations. However, they also reveal gaps in exposure to the physical examination of specific organ systems (e.g., neurological and musculoskeletal and genital-urinary systems) and in the development of communication skills. While students reported high satisfaction with their learning experience, specific areas – such as limited opportunities for hands-on procedural training and variation in speciality exposure – emerged as points for improvement.

The adherence rate to the digital logbook was remarkably high with 99.5% of students documenting their clinical activities, possibly allowing for a valuable overview of the activities practiced by the students.

The third-year rotation aimed to develop autonomous history-taking. Students were expected to write three histories followed by their discussion, but averaged five, exceeding curriculum goals. Though mandatory, only 95% logged it, likely due to underreporting, as all students fulfilled this requirement.

"General Tasks" comprehended activities that are universal to all specialties or that concern soft skills. The most logged activities were "Hand hygiene" and "Hand disinfection technique" reported by 80% and 68% of students, respectively. However, considering the fundamental importance of these activities, it is surprising that the participation level was not 100%, raising several topics for discussion. One possible explanation is underreporting, given the self-reported nature of our data collection. Additionally, previous studies have highlighted that student compliance with hand hygiene protocols has remained suboptimal, often due to gaps of knowledge regarding proper techniques and the lack of recognition of its importance in infection control.[12-14] Moreover, research has shown that trainees are heavily influenced by their role models, yet many senior physicians fail to consistently adhere to hand hygiene protocols, inadvertently setting a poor example for students.[15] Given these findings, and as suggested by available literature, repetitive hand hygiene training should be implemented into the curriculum, incorporating that both practical training and mechanisms to monitor its effectiveness, while also emphasizing the importance of positive role modelling by supervisors. [13, 15]

In contrast, "Participation in Bad News Transmission" was the least practiced activity, with only 25% students recording it. This limited involvement likely comes from the complexity and sensibility required for this task, which may be challenging for students still midway through their training.[16, 17] In fact, patient communication, particularly bad news transmission, is primarily taught later in our school's curriculum, possibly limiting students' ability to participate in real-life patient interactions where this skill is required. As reported in other studies, many medical students report feeling underprepared for delivering bad news due to a lack of structured training, with existing curricula often relying on inconsistent teaching methods.[18]

Additionally, some supervisors may be reluctant to involve junior colleagues in these conversations, as they themselves view them as emotionally distressing and may fear that the presence of inexperienced colleagues could worsen the situation.[19] However, many patients express dissatisfaction with how doctors communicate bad news, which further highlights the need for improved education in this area and early involvement of students.[20, 21]

Despite being a recommended clinical activity, student engagement in "Writing Patient Charts" under supervision, was low (54%). Gliatto et al. recognised the importance of students documenting patient encounters to develop essential skills in clinical reasoning and communication.[22] However, institutional barriers such as liability concerns and added workload for supervisors may limit student involvement. (22, 23) This reluctance, coupled with the fact that this is students' first clinical rotation, may contribute to the low participation observed. Similar findings in Germany suggest that students are less frequently given responsibility for patient documentation compared to the U.S. (24). To address this, we propose incorporating specific objectives into the rotation to encourage supervised student participation.

Standard physical examinations of "Thorax and Lungs", such as inspection, auscultation or assessment of respiratory rate, had high levels of engagement, while other traditional examinations like "Per-oral auscultation" or "Auscultation of transmitted voice sounds" proved more limited, as they might end up being replaced by modern technology.(25, 26) However, despite clinicians' beliefs that clinical imaging is a more accurate diagnostic tool than physical examination, evidence suggests otherwise. In fact, detecting changes on auscultation of voice sounds – such as those

seen in pneumonia - revealed to be more consistently recognized by different clinicians than abnormalities detected on chest radiography, reinforcing the importance of preserving these techniques in modern teaching.[27] "Per-oral auscultation", on the other hand, is a technique not commonly described in physical examination textbooks. For this reason, its inclusion in the core curriculum could be reconsidered.

Neurological, musculoskeletal, and genital-urinary exams did not exceed 65% participation, likely due to their specificity and varied clinical settings our students our placed in. As this was students' first clinical experience, future rotations will provide further training.

Regarding procedures, arterial blood gas collection was performed by very few students. This low participation rate is likely due to the greater time required for training and teaching this technique during clinical rotations. Nonetheless, practicing these procedures was not one of the main objectives of this internship, but more a complementary activity.

The assessment of activities outside the core curriculum highlights areas for potential improvement and revision of both the Student Logbook and the curriculum, ensuring that essential clinical skills are adequately emphasized in medical training. For instance, the category "Assessment of peripheral edema" was recorded by only a few students. However, this activity is considered significant enough to warrant inclusion in a future version of the Student Logbook due to its fundamental importance and routine use in clinical wards, as it is seen in a multitude of conditions. [27, 28]

The response rate for the survey, while significantly lower than logbook adherence, still offers valuable insights into students' perceptions of their clinical experience. The moderate participation may be attributed to several factors, including **survey fatigue, the perception that feedback would not lead to meaningful change, or a lack of personal incentive to complete the survey.** [29, 30]

Most students interacted exclusively with their assigned supervisor for the greater part of the rotation. This continuity likely facilitates meaningful feedback and enables supervisors to effectively monitor students' progress and skill development over time. The positive impact of sustained mentorship during clinical rotations has been well-documented in the literature, including studies such as Thistlethwaite et al.[31]

Similarly, the quality of supervision is closely tied to the supervisor's ability to balance providing students with adequate autonomy while offering necessary support for their tasks.[32, 33] In our study, this balance was reflected in the high levels of perceived support, with nearly 90% of students reporting feeling supported when taking clinical histories.

This study offers valuable insights, but several limitations should be acknowledged. Using a self-reported digital logbook may have led to inconsistencies, affecting data accuracy. Subjective feedback and categorization could introduce interpretation bias. Additionally, students may have downplayed past challenges after receiving high final evaluations.

This study was instrumental in refining and reassessing the clinical skills and techniques outlined in the curriculum, ensuring they align with students' learning needs. Additionally, our findings could serve as a basis for comparing different medical education approaches in institutions using similar logbook systems, both nationally and internationally, contributing to the progressive improvement of medical training.

Qualitative feedback revealed that some students felt their assigned medical specialty was not ideally suited to the rotation's educational objectives, raising the question of whether certain specialties provide a more conducive learning environment. The low participation in musculoskeletal, neurological, and genitourinary examinations may reflect this misalignment. Future studies could assess how different specialties contribute to core competencies, allowing for a more strategic allocation of students and optimizing their clinical experience.

Further research could explore whether these early learning gaps persist throughout medical training, whether simulation or AI-assisted teaching could complement clinical exposure, and how different educational models impact skill acquisition. Additionally, enhancing supervisor engagement in practical teaching and documentation could maximize students' hands-on involvement. Addressing these aspects would contribute to create a more structured and effective medical education, ensuring the progressive development of essential clinical competencies.

To conclude, this study demonstrated students' strong engagement in core clinical procedures and high satisfaction. However, gaps in specialty exposure, communication skills, and hands-on training in medical routines and procedural skills were identified, highlighting opportunities for improvement to ensure a more comprehensive clinical education.

SUPPLEMENTARY FILES

Appendix A – List of Available Hospitals and Departments

Hospital	Specialty/Department	Number of available spots
Beatriz Ângelo	General Surgery Internal Medicine Gastroenterolgy	10 14 8
Forças Armadas	Internal Medicine	28
Arrábida - Setúbal	Internal Medicine General Surgery	6 8
Institute of Oncology (IPO)	Head and neck surgery General Surgery	2 12
Garcia de Horta	Vascular Surgery Reumathology Nephrology Maxilo-facial Surgery Cardiology	6 4 2 2 4
Cascais	Internal Medicine	4
Fernando da Fonseca	Neurology Infecciology Nephrology Gastroenterolgy Internal Medicine Stroke Unit Cardiology	4 6 4 10 20 8 16
Santa Maria	Cardiology General Surgey Gastroenterolgy Dermatology Paediatrics Vascular Surgery Anestesiology Stomatology Emergency Medicine Nephrology Endocrinology Internal Medicine Reumathology Pneumology	22 24 4 6 12 10 6 2 2 6 6 16 4 8
Lusíadas	Orthopaedic Surgery General Surgery Intensive Medicine Internal Medicine	10 2 2 6
CUF Descobertas	Orthopaedic Surgery Anestesiology General Surgery	2 2 2
Luz Lisboa	Internal Medicine Gastroenterolgy Pneumology General Surgery	6 2 6 6
Portuguese Institute of Reumathology	Reumathology	10
Luz Setúbal	Internal Medicine	2
Barreiro-Montijo	Internal Medicine General Surgery	6 2
Santarém	Reumathology	2
Oeste	Internal Medicine	2
Aveiro	Reumathology	2

Appendix B – Original Clinical Logbook

	Logbook	n*
Geral	Aplicação da higienização das mãos	
	Aplicação da técnica de desinfeção das mãos	
	Anamnese e colheita de história clínica	
	Discussão das principais hipóteses diagnósticas	
	Discussão do diagnóstico diferencial com base em achados clínicos	
	Acompanhamento da equipa médica na visita clínica (se aplicável)	
	Colaboração no registo médico eletrónico	
	Colaboração na seleção dos MCDTs indicados a suportar as hipóteses diagnósticas	
	Consentimento informado (oral e/ou escrito)	
	Colaboração na entrevista a familiares	
	Colaboração na comunicação de más notícias	
Sistema Cardio-vascular	Cardíaco - Auscultação cardíaca	
	Geral - Avaliação dos sinais de perfusão capilar	
	Geral - Avaliação de cadeias ganglionares linfáticas	
	Cardíaco - Pesquisa de frémito	
	Cardíaco - Avaliação e interpretação do impulso apical/choque da ponta	
	Vascular - Palpação e descrição do pulso arterial	
	Vascular - Medição da pressão arterial	
Sistema Respira-tório	Auscultação dos sons pulmonares e ruídos adventícios	
	Inspeção do tórax	
	Avaliação da frequência respiratória	
	Avaliação do padrão respiratório	
	Deteção de sinais de dificuldade respiratória	
	Percussão da parede torácica anterior, posterior e lateral	
	Avaliação da expansibilidade torácica	
	Avaliação das vibrações vocais	
	Auscultação per-oral	
	Auscultação da voz	
Sistema Neuroló-gico	Avaliação das funções nervosas superiores	
	III, IV e VI - Oculomotores	
	VII - Facial	
	Avaliação da força muscular - Global	
	Avaliação da força muscular - Segmentar	
	II - Ótico	
	V - Trigémio	
	XII - Hipoglosso	
	Avaliação do tónus muscular	
	Avaliação da sensibilidade	
	Avaliação das funções vestíbulo-cerebelosas	
	XI - Espinhal	
	IX e X - Glossofaríngeo e vago	
	VIII - Acústico	
	Avaliação de reflexos - Ósteo-tendinosos	

	Pesquisa de sinais meníngeos	
	Pesquisa do Sinal de Lasègue	
	Avaliação de reflexos - Cutâneos	
	Pesquisa do Sinal de Babinsky	
Sistema Digestivo	Inspeção do abdomén	
	Palpação da parede abdominal	
	Percussão da parede abdominal	
	Auscultação dos ruídos hidroaéreos	
	Avaliação de sinais de irritação peritoneal	
	Pesquisa do Sinal da Onda líquida	
	Pesquisa do Sinal de Murphy renal	
Sistema Músculo--esquelético	Avaliação das articulações do punho e mão	
	Estudo da marcha	
	Avaliação da articulação do joelho	
	Avaliação da articulação do cotovelo	
	Avaliação da articulação do tornozelo e pé	
	Avaliação da articulação do Ombro	
	Avaliação da Coluna vertebral	
	Avaliação da articulação coxo-femoral	
	Avaliação das articulações sacro-ilíacas	
Sistema génito--urinário	Inspeção e palpação mamária	
	Inspeção perianal e toque retal	
Cabeça	Avaliação da orofaringe	
	Palpação dos seios perinasais	
	Inspeção do nariz e das fossas nasais	
	Inspeção e palpação do ouvido e otoscopia	
Técnicas/ pequenos gestos	Avaliação de radiografia simples	
	Execução e interpretação de eletrocardiograma	
	Gasimetria arterial	
Outras Atividades	Texto livre	

** n = Número total de procedimentos realizados*

Appendix C – Online Survey *(translated to english)*

Dear students,

With this brief anonymous questionnaire, we aim to gather informal feedback regarding your satisfaction and learning experience during your internship.

All questions are optional, including those about your tutor, department, and hospital. However, when relevant, we kindly ask you to identify at least the department/hospital to help us better assess the internship experience across different institutions.

Any individual results that could identify a tutor, department, or hospital will remain strictly confidential and accessible only to the course administration.

We appreciate your responses by **July 31**.
Thank you!

1. Hospital where the internship was conducted
2. Department where the internship was conducted
3. Name of the official tutor
4. Besides your official tutor, did you spend more than 50% of your internship with another doctor?
   ☐ Yes (please specify at the end if you believe this doctor should be invited as an official tutor)
   ☐ No
   ☐ Other: _____
5. Did you feel supported in conducting clinical histories?
   ☐ Yes
   ☐ No
   ☐ Other: _____
6. Did you have the opportunity to perform minor procedures (e.g., venous blood collection, blood gas analysis, etc.)?
   ☐ Yes
   ☐ No
   ☐ Maybe
7. Did you have the opportunity to provide clinical information to patients' family members?
   ☐ Yes
   ☐ No
   ☐ Maybe
8. Were you responsible for entering electronic medical records?
   ☐ Yes
   ☐ No
   ☐ Maybe
9. Satisfaction with the team's reception, friendliness, and integration
   ☐ Very poor 1 2 3 4 5 Excellent
10. Satisfaction with the knowledge and clinical skills acquired during the internship
    ☐ Very poor 1 2 3 4 5 Excellent
11. Would you recommend your tutor to your colleagues?
    ☐ Yes
    ☐ No
    ☐ Maybe
12. Would you recommend the department where you interned to your colleagues?
    ☐ Yes
    ☐ No
    ☐ Maybe
13. Would you recommend the hospital where you interned to your colleagues?
    ☐ Yes
    ☐ No
    ☐ Maybe
14. Satisfaction with the Xerpa application and internship logbook
    ☐ Not satisfied 1 2 3 4 5 Very satisfied
15. Positive aspects of your internship: _____
16. Negative aspects of your internship: _____

SUPPLEMENTARY FILES

Appendix D – Data categorization

The data from digital logbook was exported to Microsoft Excel for organization and analysis. A total of 72 Core Clinical Procedures were grouped into categories based on their corresponding medical specialties. Additional procedures, recorded as free-text entries by students, were consolidated into distinct categories, such as observation or participation in surgeries, or participation in teaching sessions (table D.1).

This categorization was necessary because students often described similar experiences using varied language, leading the app to register them as separate entries. For instance, all observations of ambulatory consultations, regardless of specialty, were grouped under "Observation of Ambulatory Consultations." The same approach was applied to other experiences, such as surgeries, teaching sessions, and meetings. This process ensured consistency and improved the clarity of the data, enabling a more accurate analysis of students' activities during the internship.

Regarding the survey analysis, positive and negative feedback (table D.2 and table D.3) regarding the rotations, collected as free-text entries, were also categorized into distinct themes for the same reason. Positive feedback was grouped into themes such as mentorship, learning experience, and team-integration, while negative feedback was categorized into themes such as lack of supervisor support, limited clinical variety, or lack of hands-on practice.

Table D.1 – Categorization of activities outside the curriculum

Activities outside the core curriculum	Example entry
Observation/ practicing of techniques/ procedures specific to specialty	*"Observation of endoscopic procedures"; "I helped ventilate the patient"*
Observation of surgeries	*"Watched mamma surgery"; "Watched cataract surgery"*
Physical examinations outside core curriculum	*"Palpation of the testicules"; "Assessment of Pemberton sign"*
Observation of ambulatory consults	*"Participation in mamma oncology consults"; "I was in cardiology consults"*
Observation/ participation in clinical teaching session	*"I watched a clinical session on oesophageal rupture"*
Minor surgery	*"I helped with minor surgery procedures"*
Observation of emergency room shifts	*"I went to the ER with my supervisor"*
Participation in surgeries	*"I scrubbed in a testical tortion surgery"*
Venous punctures	*"I practiced venous punctures"*
Assessment of peripheral edema	*"I assessed peripheral edema"*
Observation of department meetings	*"I watched department meetings"*
Observation of MDT meetings	*"I was in MDT meetings for oncology patients"*

Note: Free text entries that not met any of these categories was removed as it was considered to be very low frequency and not relevant for the objectives of the study.

Table D.2 – Categorization of Positive Feedback

Category of positive feedback	Example Comments
Enriching Learning Experience	*"I got to test my own knowledge with the help of my tutor on a patient's bedside"*
Supportive Mentorship	*"I learned a lot with my Tutor, who was always available to help"*
Effective Rotation Organization	*"They were very flexible with the scheduling"*
Collaborative Team Environment	*"The whole department was very welcoming and always explained what was going on"*
Optimized Learning Facilities	*"The hospital was calm which allowed for a better learning experience"*
Personal Growth and Confidence Building	*"I was given autonomy within the limitations of still being a student"*
Other	*"The hospital was close to my home"*

Table D.3 – Categorization of Negative Feedback

Category of negative feedback	Example Comments
Insufficient Mentorship	"We didn't have a lot of support… our tutor never had any time"
Excessive Workload	"The rotation was too long"
Limited Clinical Practice Variety	"I was only in consultations and only observing"
Lack of Team Integration	"A lot of times we were left alone without any guidance"
Organizational Issues	"My tutor had to many students as many assigned tutor had left on holidays"
Skill Development Gaps	"I didn't get to practice any procedures of the logbook"
Medical Specialty was not adequate for this rotation	"*[the speciality] is ioo specific for 3rd year students*"
Negative Xerpa App feedback	"*I don't understand the need to use Xerpa*"
Other	"*It was hard to get to the hospital without a car*", "*The evaluation was not fair compared to others*"

Other Comments regarding the use of Xerpa:

"As there was a separate category called "clinical histories" I thought I was supposed to put the information gathered through the 3 histories. For me and my colleague it wasn't clear that we had to write notes on the different patients we observed. Only at the end of the internship. We suggest for future years this information is clearer."

"Registering [clinical histories] in Xerpa does not help with this rotation. Since we must fill out the information about the patients as we talk with them, it does not a good impression to be using the phone."

CONFLICT OF INTERESTS:

The authors have no conflict of interests to declare.

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Diplexil R

Valproato Semisódico

CONFIANÇA NUMA VIDA COM QUALIDADE[1,2]

INFORMAÇÕES ESSENCIAIS COMPATÍVEIS COM O RESUMO DAS CARACTERÍSTICAS DO MEDICAMENTO

▼Este medicamento está sujeito a monitorização adicional. Isto irá permitir a rápida identificação de nova informação de segurança. Pede-se aos profissionais de saúde que notifiquem quaisquer suspeitas de reações adversas. Para saber como notificar reações adversas, ver secção 4.8 do RCM.

NOME, COMPOSIÇÃO QUALITATIVA E QUANTITATIVA e FORMA FARMACÊUTICA DO MEDICAMENTO: Diplexil-R 250 mg (269,1 mg de valproato semisódico) comprimidos gastrorresistentes cor de pêssego. Excipiente(s) com efeito conhecido: Amarelo sunset (E110) – 0,2 mg, Sódio: 18,5 mg por comprimido. Diplexil-R 500 mg (538,2 mg de valproato semisódico) comprimidos gastrorresistentes cor-de-rosa. Excipiente(s) com efeito conhecido: Carmoisina (E122) - 0,104 mg, Vermelho de ponceau 4R (E124) - 0,091 mg, Sódio: 37,0 mg por comprimido. **INDICAÇÕES TERAPÊUTICAS:** Epilepsias generalizadas e parciais: Generalizadas primárias: Pequeno e grande Mal, epilepsias mioclónicas; Parciais: simples e complexas. Generalizadas secundárias: síndroma de Lennox-Gastraut, síndroma de West; Formas mistas. Epilepsias especiais: Convulsões febris na criança. Privação do sono. Alterações do comportamento associados à epilepsia. Tratamento de episódios maníacos na doença bipolar quando o lítio está contraindicado/ não é tolerado. Considerar a continuação do tratamento após a ocorrência de episódios maníacos em doentes que responderam ao valproato semisódico na mania aguda. Em: Doentes com ciclos rápidos; bipolares difíceis (idosos e doentes em situações de comorbilidade com abuso de substâncias). - Tratamento profilático dos seguintes tipos de cefaleias: Enxaqueca, Cefaleia Crónica Diária (Enxaqueca Transformada e enxaqueca Persistente e Resistente) e Cefaleia em salvas. **POSOLOGIA E MODO DE ADMINISTRAÇÃO:** Via oral. Se tratamento prévio com Ácido valpróico, iniciar a terapêutica com a mesma dose diária e esquema posológico. Após estabilização do doente poderá instituir-se um esquema posológico de 2 a 3 tomas diárias. A frequência de efeitos adversos (particularmente enzimas hepáticas elevadas) pode estar relacionada com a dose. Avaliar benefício-risco de doses mais elevadas. Concentrações de Fenitoína no sangue podem ser afetadas com aumento de dosagem. Para os doentes que se queixam de irritação gastrointestinal, recomenda-se a administração do fármaco durante as refeições, e aumento gradual da dose a partir de um nível inicial baixo. Epilepsia: dose inicial recomendada:15 mg/kg/dia 3 x dia, com aumentos de 5 a 10 mg/kg/dia em intervalos de uma semana até controlo das crises ou até dose tolerável. A dose máxima recomendada é de 60 mg/kg/dia. Se exceder os 2500 mg, esta deverá ser administrada em doses repartidas. Para a maior parte dos doentes, as concentrações séricas terapêuticas de Valproato situam-se no intervalo de 50-100 mcg/ml. Caso a posologia diária seja igual ou superior a 50 mg/Kg/dia, recomenda-se monitorizar níveis sanguíneos. Episódios maníacos na doença bipolar: Em adultos: A dose diária deve ser estabelecida e controlada pelo médico. Dose diária inicial recomendada é de 750 mg. Em ensaios clínicos, a dose inicial de 20 mg de valproato/kg de peso corporal também demonstrou um perfil de segurança aceitável. A dose deve ser aumentada tão rapidamente quanto possível, de forma a atingir a dose terapêutica mais baixa que produza o efeito clínico desejado. Ajustar a dose à resposta clínica. A dose média diária varia, habitualmente, entre 1000 a 2000 mg de valproato. Se doses superiores a 45 mg/kg de peso corporal, monitorizar. A continuação do tratamento deve ser adaptada individualmente usando a dose mínima eficaz. Em crianças e adolescentes: A segurança e a eficácia de Diplexil-R para o tratamento de episódios maníacos na doença bipolar não foram avaliadas em doentes com idade inferior a 18 anos. Crianças do sexo feminino e mulheres em idade fértil: O valproato deve ser iniciado e supervisionado por um especialista com experiência no tratamento da epilepsia, perturbação bipolar ou enxaqueca. O valproato não deve ser utilizado em crianças do sexo feminino e mulheres em idade fértil a não ser que outros tratamentos sejam ineficazes ou não tolerados. O valproato é prescrito e dispensado de acordo com o Programa de Prevenção do valproato na Gravidez. O valproato deve ser prescrito preferencialmente em monoterapia e na dose eficaz mais baixa, se possível numa formulação de libertação prolongada. A dose diária deve ser dividida pelo menos em duas tomas únicas. Homens: Recomenda-se que Diplexil seja iniciado e supervisionado por um especialista com experiência no tratamento da epilepsia ou perturbação bipolar ou enxaqueca. Cefaleias: A dose mínima eficaz é de 250 mg 2x dia e o tratamento deverá ter a duração mínima de 3 meses. A dose média é de 1000 a 1500 mg/dia. Em doentes com insuficiência renal: pode ser necessário diminuir a dosagem, ou aumentar a dosagem em doentes em hemodiálise. Valproato é dialisável. A dosagem deve ser modificada de acordo com a monitorização clínica do doente. Diplexil-R só deve ser iniciado e supervisionado por um especialista com experiência no tratamento da enxaqueca. O tratamento só deve ser iniciado se outros não forem eficazes ou tolerados e os benefícios e riscos devem ser cuidadosamente reavaliados em revisões regulares do tratamento. **CONTRAINDICAÇÕES:** Diplexil-R está contraindicado nas seguintes situações: - Hipersensibilidade às SA ou excipientes. - Doença hepática ou disfunção significativa. - Antecedentes pessoais ou familiares de hepatite grave, nomeadamente medicamentosa. - Porfiria hepática. - Doentes que tenham doenças mitocondriais causadas por mutações no gene nuclear que codifica a enzima mitocondrial polimerase gama (POLG), por exemplo a síndrome de Alpers-Huttenlocher, e em crianças com menos de 2 anos de idade em que se suspeita de terem doenças relacionadas com a POLG. - Doentes com distúrbios do ciclo da ureia. Tratamento da epilepsia: - Na gravidez, a não ser que não exista um tratamento alternativo adequado. - Em mulheres em idade fértil, a não ser que as condições do programa de prevenção da gravidez sejam cumpridas. Tratamento da perturbação bipolar e profilaxia de crises de enxaqueca: - Na gravidez. - Em mulheres em idade fértil, a não ser que as condições do programa de prevenção da gravidez sejam cumpridas. **ADVERTÊNCIAS E PRECAUÇÕES ESPECIAIS DE UTILIZAÇÃO:** trombocitopénia, alterações da hemostase/coagulação, hiperamonemia com ou sem letargia, alterações nos testes de função da tiroide, insuficiência hepática, muito raramente pancreatites graves, reações adversas cutâneas graves e angioedema. **Programa de Prevenção de Gravidez:** O valproato tem um elevado potencial teratogénico e as crianças expostas ao valproato in utero têm um elevado risco de malformações congénitas e perturbações do desenvolvimento do sistema nervoso. Ver RCM. Foram relatados casos de ideação e comportamentos suicidas em doentes tratados, com medicamentos antiepiléticos, para várias indicações terapêuticas. Não é recomendado o uso concomitante de ácido valpróico/ valproato de sódio com os antibióticos do grupo dos cabapenemos. Doentes com doença mitocondrial conhecida ou presumida: O valproato pode desencadear ou agravar sinais clínicos de doenças mitocondriais subjacentes causadas por mutações do ADN mitocondrial bem como do gene nuclear que codifica a POLG. Se há suspeita de uma deficiência no ciclo enzimático da ureia, devem ser feitos estudos metabólicos antes do tratamento, devido ao risco de hiperamoniemia com o valproato. Poderá ocorrer aumento de peso no início do tratamento. Doentes com uma deficiência tipo II em carnitina palmitoiltransferase subjacente (CPT) devem ser advertidos do risco aumentado de rabdomiólise. Nos insuficientes renais pode ser necessário proceder-se a uma diminuição da dosagem. Excipientes. **INTERAÇÕES MEDICAMENTOSAS E OUTRAS FORMAS DE INTERAÇÃO:** Efeitos do valproato semisódico nos outros medicamentos: Neurolépticos, antidepressivos, benzodiazepinas e barbitúricos; Fenobarbital e Primidona; Fenitoína; Carbamazepina; Etossuximida; Lamotrigina; Zidovudina; Felbamato; Olanzapina; Rufinamida; Propofol; Nimodipina. Efeito de outros medicamentos sobre o valproato de sódio: Antiepiléticos; Mefloquina; Fármacos com ligação elevada às proteínas plasmáticas; Anticoagulantes; Cimetidina ou eritromicina; Fluoxetina; Carbapenemos; Rifampicina; Inibidores de protéase; Colestiramina; Medicamentos que contêm estrogénio; Metamizol; Outras interações: Topiramato ou acetazolamida; Quetiapina; Álcool; Lítio; Clonazepam; Clozapina. Ver RCM. **EFEITOS INDESEJÁVEIS:** Os efeitos indesejáveis notificados mais comuns para o valproato são perturbações gastrointestinais, as quais ocorrem em aproximadamente 20% dos doentes. Têm sido observados casos de lesões hepáticas graves (ou mesmo fatais), especialmente em crianças tratadas com doses elevadas ou em combinação com outros antiepilépticos. Os efeitos indesejáveis foram classificados por ordem de frequência segundo a seguinte convenção: Neoplasias benignas, malignas e não especificadas (incl. quistos e polipos): Raros: Síndrome mielodisplásico. Doenças do sangue e do sistema linfático: Frequentes: Trombocitopenia, leucopenia. Pouco frequentes: Hemorragia. Raros: Anemia macrocítica, macrocitose. Muito raros: Perturbações da medula óssea, concentração reduzida de fibrinogénio e/ou de fator de coagulação VIII, alteração da agregação plaquetária, tempo de coagulação prolongado, linfocitopénia, neutropénia, pancitopénia, anemia ou aplasia da linhagem de células vermelhas. Desconhecido: Agranulocitose. Doenças do sistema imunitário: Pouco frequentes: Angioedema. Raros: Lúpus eritematoso, erupção medicamentosa com eosinofilia e sintomas sistémicos (síndrome DRESS). Desconhecido: Reações alérgicas (ver também "pele e perturbações dos tecidos subcutâneos"), síndrome da resposta inflamatória sistémica. Doenças endócrinas: Raros: Hiperandrogenismo (hirsutismo, virilismo, acne, alopécia com aparência típica masculina e/ ou aumento dos níveis de androgéneos), hipotiroidismo. Doenças do metabolismo e da nutrição: Frequentes: Hiperamonemia, aumento do peso (fator de risco para a síndrome do ovário poliquístico, requer monitorização cuidadosa) ou diminuição de peso; aumento ou diminuição de apetite. Pouco frequentes: Síndrome de secreção inapropriada de hormona antidiurética (SIADH). Raros: Hiperinsulinemia, baixos níveis da IGFBP-1 (insulin-like growth factor binding protein 1), obesidade. Muito raros: Foram relatadas anomalias das provas da função tiroideia, com relevância clínica duvidosa. Hiponatremia. Vasculopatias: Raros: Vasculites. Perturbações do foro psiquiátrico: Frequentes: Agressividade*, agitação*, atenção alterada*. Raros: Irritabilidade, alucinações, confusão, comportamento anormal*, hiperatividade psicomotora*, perturbação da aprendizagem*. * Estas reações adversas são observadas principalmente na população pediátrica. Doenças do sistema nervoso: Frequentes: Sonolência, tremores, parestesias, defeito de memória, nistagmo, torturas. Pouco frequentes: Coma transitório, em alguns casos associado a aumento da frequência das crises, ataxia. Raros: Cefaleias, hiperatividade, espasticidade, estupor, perturbação cognitiva, diplopia. Muito raros: Encefalopatia, demência associada a atrofia cerebral (reversível após a descontinuação do tratamento), distúrbios extrapiramidais p. ex. síndrome parkinsónica (reversível). Desconhecido: Agravamento das crises, sedação, letargia. Afeções do ouvido e do labirinto: Muito raros: Perda de audição (reversível ou irreversível), acufenos. Doenças respiratórias, torácicas e do mediastino: Pouco frequentes: Derrame pleural (eosinofílico). Doenças gastrointestinais: Muito frequentes: Dores, náuseas, vómitos. Frequentes: Diarreia, perturbação gengival (principalmente hiperplasia gengival), estomatite. Raros: Pancreatite (por vezes fatal), hipersalivação, ileus, obstrução intestinal. Afeções hepatobiliares: Frequentes: Alterações nas provas da função hepática. Raros: Lesão hepática grave que inclui insuficiência hepática. Afeções dos tecidos cutâneos e subcutâneos: Frequentes: alopecia, enfraquecimento do cabelo e aparecimento de cabelo encaracolado, alterações nas unhas e leito ungueal. Raros: Exantema, eritema multiforme. Muito raros: Síndrome de Stevens-Johnson, Síndrome de Lyell. Desconhecido: Hirsutismo (por ex. resultante da síndrome do ovário poliquístico), hiperpigmentação. Afeções musculosqueléticas e dos tecidos conjuntivos: Raros: Rabdomiólise. Desconhecido: Foram notificados casos de densidade mineral óssea diminuída, osteopenia, osteoporose e fraturas ósseas em doentes sob tratamento prolongado com valproato. Ainda não se conhece o mecanismo pelo qual o valproato afeta o metabolismo ósseo. Doenças renais e urinárias: Frequentes: incontinência urinária. Muito raros: Síndrome de Fanconi (com acidose metabólica, fosfatúria, aminoacidúria, glicosúria, reversíveis após a descontinuação do tratamento), enurese nas crianças. Desconhecido: Insuficiência renal, nefrite intersticial, deterioração da função renal. Doenças dos órgãos genitais e da mama: Frequentes: Amenorreia, dismenorreia. Raros: Síndrome de ovário poliquístico, infertilidade masculina. Desconhecido: Espermatogénese anormal (com contagem reduzida de espermatozóides e/ou motilidade). Afeções congénitas familiares e genéticas: Malformações congénitas e alterações no desenvolvimento. Perturbações gerais e alterações no local de administração: Raros: Hipotermia, edema. Exames complementares de diagnóstico: Raros: Redução dos fatores de coagulação (pelo menos um), testes de coagulação anormais (tais como prolongamento do tempo de protrombina, prolongamento do tempo parcial de tromboplastina ativada, prolongamento do tempo de trombina, valor de INR aumentado), carência de biotina/biotinidases. População pediátrica: Existe risco particular de lesão hepática grave em bebés e crianças pequenas, especialmente com idade inferior a 3 anos, e de pancreatite em crianças pequenas. Estes riscos diminuem com o aumento da idade. Transtornos psiquiátricos como agressão, agitação, perturbação da atenção, comportamento anormal, hiperatividade psicomotora e transtorno de aprendizagem são observados principalmente na população pediátrica. **Para mais informações deverá contactar o Titular da AIM:** TECNIFAR - Indústria Técnica Farmacêutica, S.A. Rua José Da Costa Pedreira, Nº 11 – B - Torre Sul - 1750-130 Lisboa. **Medicamento sujeito a receita médica.** Regime de comparticipação: Escalão A. **RCM aprovado a 05-02-2025 (versão 24.0)**

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TECNIFAR

CLINICO-PATHOLOGICAL CASE

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

Remission of Parkinson's Disease Rest Tremor Following Cerebellar Hemorrhage

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ABSTRACT: Parkinson's Disease (PD) is a clinical diagnosis that relies on the presence of bradykinesia and rigidity and/or rest tremor. Whereas the striatal dopamine depletion explains the characteristic PD symptoms such as bradykinesia and rigidity, the mechanism of tremor generation is not completely established. Mounting evidence suggests that resting tremor is associated with increased activity in a distinct cerebellothalamic circuit, which may explain its lower response to dopaminergic treatment.

We describe the case of a 74-year-old man with idiopathic tremor-dominant PD who experienced rest tremor remission after cerebellar hemorrhage, supporting the role of the cerebellum in rest tremor pathophysiology.

KEY WORDS: Parkinson's Disease; Rest Tremor; Cerebellar Hemorrhage

INTRODUCTION

The clinical diagnosis of PD relies on bradykinesia and rigidity and/or rest tremor.[1] Neuronal loss in the substantia nigra and intracellular inclusions containing aggregates of α-synuclein are its neuropathological hallmarks resulting in dysfunction of striato-thalamo-cortical pathways.[2] However, considering the anatomical connections between the cerebellum and basal ganglia[3] and the increased activation of the cerebellum found in individuals with PD, it has been suggested that the cerebellum may also contribute to the pathophysiology of PD symptoms, mainly tremor.[2,4,5] We describe a case of PD rest tremor remission after ipsilateral cerebellar hemorrhage, which may support the role of the cerebellum in rest tremor pathophysiology.

CASE REPORT

A 74-year-old man, right-handed, with a history of smoking and localized prostate adenocarcinoma, was followed in our neurology outpatient clinic for idiopathic tremor-dominant Parkinson's Disease with 11 years of evolution and a Hoen & Yahr scale of 2. The neurologic

examination revealed upper and lower limbs moderate rigidity and bradykinesia as well as a disabling, high amplitude, pill-rolling and flexion-extension rest tremor in the right upper limb, without postural or intentional components (UPDRS-III tremor 7), and minor gait impairment. At that time, the patient was undergoing treatment with Levodopa/Benserazide 800 mg/day, Levodopa/Benserazide CR 100 mg/day, Rasagiline 1 mg/day, and Opicapone 50 mg/day. A few months after the last follow-up visit, the patient was admitted to the emergency department (ED) with occipital headache, vomiting, and gait instability. At ED admission blood pressure was 170/89 mmHg. Neurological evaluation revealed somnolence and mild paresis on the right upper limb (NIHSS 2). A brain MRI revealed a corticosubcortical in the right cerebellar hemisphere, with a maximum dimension of 5.4 cm along its longest axis, with extension to the medial cerebellar peduncle and the superior portion of the vermis, along with a slight deviation of the fourth ventricle (Figure 1). A hypertensive etiology was assumed, and treatment with an angiotensin-converting enzyme inhibitor and a calcium channel blocker was initiated. At the follow-up visit, six months after the stroke, the resting tremor had disappeared (UPDRS-III tremor score: 0), as confirmed by both the examiner and the patient.

DISCUSSION

Resting tremor is the classic type of tremor in PD. Whereas the striatal dopamine depletion explains the characteristic PD symptoms such as bradykinesia and rigidity, increasing evidence suggests that resting tremor is associated with increased activity in a distinct cerebellothalamic circuit, justifying its lower and unpredictable response to dopaminergic treatment. [2,4,6]

Growing data support the role of the cerebellum in Parkinson's disease. A "dimmer-switch model" was proposed to explain tremor generation. According to the dimmer-switch hypothesis, tremor-related activity originates at the internal pallidal globus, which propagates to the cortex. The cortex and ventral intermediate nucleus of thalamus (VIM) form a circuit, which is possibly the base of tremor-related oscillation. The cerebellum also projects to VIM, with this projection possibly modulating amplitude of tremor, while cerebellum is modulated by cerebral cortex. Multiple neurotransmitter systems are involved, including the dopaminergic retrorubral area, noradrenergic locus coeruleus, and serotonergic raphe nuclei.[7,8,9] So, this model suggested that tremor onset involves basal ganglia circuitry, whereas tremor magnitude involves cerebellar-thalamocortical projections.

Lewis et al, 2011, also investigated the role of the cerebellum in PD by studying functional differences between PD subtypes using fMRI, suggesting that the primary dysfunction in the cerebellar-thalamo-cortical circuit, particularly in the vermis and paravermis, could be responsible for the generation of resting tremor [10]. Wu et al. (2013) contributed to this understanding by using neuroimaging to demonstrate altered cerebellar activation in Parkinson's disease patients during motor execution, motor learning, and at rest, suggesting a significant role of the cerebellum in the pathophysiology of PD.[2] This was enhanced by Liu et al., 2013, who found disrupted connectivity of the dentate nucleus in

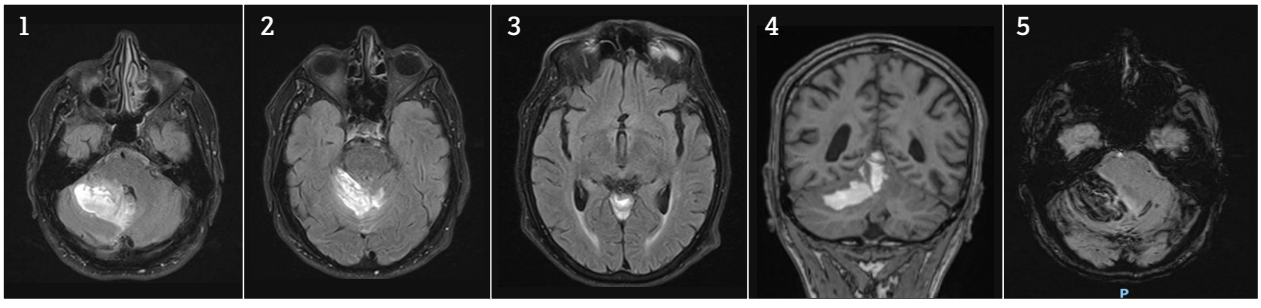

FIGURE 1. Brain MRI (1,2,3: Axial Flair, 4: Coronal T1, 5: SWI): Corticosubcortical hemorrhage in the right cerebellar hemisphere with extension to the right medial cerebellar peduncle and superior portion of vermis.

PD compared with healthy controls [11]. Bostan et al., 2013 reinforced this relation, demonstrating reciprocal connections between the basal ganglia and cerebellum via the thalamus and pontine nucleus, identifying projections between the cerebellar cortex and subthalamic nucleus via the pontine nucleus, and between the dentate nucleus and striatum via the thalamus.[3]

Lewis et al., 2013, pointed the oscillatory bursting at tremor frequencies in the VIM in PD patients consistent with its role in tremor genesis and/or propagation, with the VIM mainly receiving cerebellar inputs; and the improvement of tremor after surgical lesions or long-term stimulation of the VIM but not of bradykinesia and/or rigidity.[12] Lefaivre et al., 2016, through a repetitive transcranial magnetic stimulation protocol, demonstrated that the severity of resting tremor was reduced in individuals with tremor-dominant PD regardless of whether stimulation was applied over the medial or lateral cerebellum, suggesting involvement of the cerebellum in the generation of resting tremor.[5]

Recently, pathological changes in cerebellum have been found in PD patients. The cerebellum is affected by α-synuclein-formed Lewy bodies and by iron accumulation, which may induce white matter damage and structural and functional change. PD patients with rest tremor presented decreased gray matter volume mainly in quadrangular lobe and declive, and tremor-dominant PD patients had decreased gray matter volume in left cerebellar lobule VIIIa compared with akinesia/rigidity-dominant PD patients. Furthermore, larger volume of cerebellar lobule IV is associated with more severe resting tremor in all PD patients. These findings suggest a possible relation between these cerebellar regions and tremor in PD. Functional changes were also proved, being the functional connectivity between dentate nuclei and the cerebellar posterior lobe positively correlated with tremor severity. It seems that dentate nuclei plays a key role in cerebellum-related tremor regulation. It is possible that the activation of dentate nuclei or increase of dentate nuclei-cerebellar cortex interaction may enhance tremor. Moreover, cerebellar lobules may be involved in the mechanism of tremor in PD via its influence on dentate nuclei activity. [8]

Although the mechanism of tremor generation it is not completely established and some of the existing studies are controversial about the role of cerebellum, the majority supports a relation between tremor in PD and cerebellum, which is reinforced by our clinical report.

A deeper understanding of increased cerebellar activity, its mechanisms and effects in PD may provide a wider range of therapeutic targets, mainly for symptoms less responsive to dopaminergic treatments as tremor.

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HISTORICAL ARTICLE

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Dementia in ancient literature in Portugal

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ABSTRACT: It is generally accepted that the concept of dementia, in the present clinical meaning, is largely due to the works of the French physicians at the end of the 18th century. However, it must be recognized that the term had been previously used in literature. In the present work, we investigated in a systematic way the use of the term *demência* in old literature in Portugal.

The site *Biblioteca Nacional Digital* was searched for. The terms used were *demência, demente*. The temporal interval was from the start until 1800.

Forty-two books were found on diverse topics including poetry, religion, theatre, politics, philosophy, law and medicine. The terms *demência, demente* were usually equivalent to madness, or departure from reason, but remarkably in some cases the meaning was quite close to the present clinical concept of dementia.

KEY WORDS: Dementia; Literature; Portuguese; History

INTRODUCTION

The word *demência* comes from the latin, *de* and *mens*, meaning deprived of the mind, of reason.[1] It is considered to have been used for the first time by Aulus Cornelius Celsus (1st century)[2,3] in his book *De Medicina* (Book II.8.42).[4] Commenting on quartan fever, Celsus writes: *Si sanguis profluit, dein secuta est dementia cum distentione nervorum, periculum mortis est* (There is danger of death if haemorrhage is followed by dementia and spasm). Also in the context of fever, he refers to *insania*, which the Greeks call *phrenesis* (Book III.18.3), and explains: *Phrenesis vero tum demum est, cum continua dementia esse incipit, cum aeger, quamvis adhue sapiat, tamen quasdam vanas imagines accippit; perfecta est, ubi mens illis imaginibus addicta est* (But insanity is really there when a continuous dementia begins, when the patient, although up till then in his senses, yet entertains certain vain imaginings; the insanity becomes established when the mind becomes at the mercy of such imaginings).

It is generally accepted that the concept of dementia, in the present clinical meaning, is largely due to the works of the French physicians Philippe Pinel (1745–1826) and his disciple Jean-Étienne Dominique Esquirol (1772–1840), at the end of the 18th century.[5,6] However, it must be recognized that the term had been previously used in literature, interchanging with other more or less equivalent words.[7]

In the present work, we investigated in a systematic way the use of the term *demência* in the literature in Portugal until the end of 18th century, when the present concept was established, in order to understand its early meanings and contexts.

METHODS

The site *Biblioteca Nacional Digital* provides free and universal online access to digital contents of manuscripts and printed documents from the collections of *Biblioteca Nacional de Portugal* as well as other Portuguese libraries. It was searched for in https://bnd-digital.bnportugal.gov.pt/ (1st March 2025). The terms used were *demência, demente*. The temporal interval was from the start until 1800.

RESULTS

The online search at *Biblioteca Nacional Digital* for *demência* returned 92 results. In 66 of these, the term was in fact not demência (in all cases it was *clemência*) and were excluded. The online search for *demente* returned 186 results. In 170 occasions, the term found was not *demente* (frequently it was *grandemente*) or references had already been identified in the search for *demência*, and were excluded. Thus, we finally obtained 42 results that are shown in Table 1. These books are on very diverse topics including poetry, religion, theatre, politics, philosophy, law, or medicine (Table 1).

DISCUSSION

The term *demência* was found in the Portuguese literature a long time before the present clinical concept predominantly influenced by the French medical doctors at the end of the 18th century.

The term *demência / demente* was often used when one is out of reason due to passions like love [Table: 3, 18, 20], anger [Table: 17] vainglory [Table: 7], impatience [Table: 2], stinginess [Table: 29], or envy [Table: 24]. The term *demência* was in fact often equivalent to madness [Table: 14, 17, 38, 41].

From another perspective, the person may choose a false religion or believe in Magic [Table: 1, 6, 19, 23, 40], the Prince who does not rule in a balanced way [Table: 9], the servant may go against a powerful lord [Table: 13], one may make unfair decisions [Table: 22], endorse wrong opinions [Table: 30], or undertake unfounded expectations or wishes towards life [Table: 5, 11] and thus they fall into dementia, that is, they no longer follow reason.

Sometimes the term *demência* is obviously used with a facetious purpose [Table: 4, 8, 27].

Demência is also used in aphorisms, like the superb Seneca's sentence [Table: 12]. Also, old men, when demented, do not come to their senses [Table: 35], and what the madmen wish, they also fear [Table: 39].

Interesting legal circumstances are mentioned, the madman should not be subjected to the law when demented [Table: 15]. A man simulated a power of attorney from his demented brother to receive some ecclesiastical revenues [Table: 31]. An *Almoxarife* became demented, was unable to fulfil his duties, accumulated debts to the *Fazenda Real,* and ultimately died [Table: 33].

Remarkably, sometimes the term *demência* appears very close to what we nowadays consider the dementia syndrome. The mention to the disease of King D. Afonso VI (Lisboa, 21st August 1643 – Sintra, 12th September 1683) in the Index [Table: 10] is particularly interesting. He suffered a malignant fever when he was about four years old, was at the edge of death, and as a consequence he could not see or hear on the right side, or move the right hand and foot.[8] On the contrary, in the book cited in the Index, *Academia dos Humildes e Ignorantes,* left hemiplegia is mentioned,[9] that really seems more compatible with the portrait of the *Infante* (Figure 1). If we accept that a decline in psychosocial development was observed at this age, then the term demência would be appropriate by modern clinical standards. The cognitive damage of the *Infante* is clear, in spite of having competent teachers he could neither read nor join the letters together. The same book *Academia dos Humildes, e Ignorantes*, cited in the Index [Table: 10] describes behaviour disturbances of the king (acclaimed on the 15th November 1656) in adolescence. He would expose himself to undue perils, day and night, joining disgraceful people, whereas he should learn about how to rule the kingdom, and take care of his poor health instead.[10] In another passage, the king rudely refuses to meet his fiancé arriving from France . The court physician, António da Mata, and the surgeon, Francisco Nunes, made a written report stating that D. Afonso VI was *mentecapto e impotente*.

The case referred in [Table: 16] is also worthwhile discussing. A presumably old nun in the convent of Santa Clara de Vila do Conde, called *Veneravel Berengaria*, was considered by the other nuns as inept and demented. However, in the confusing election for Abbess in 1518, they voted for her just as an outrage. They laughed at the absurd result of the election. The old lady may

TABLE 1. Relevant records found in the Biblioteca Nacional Digital for 'Demência' and 'Demente'"

N	Book	Year	Page	Type	Passage
1	*Pelo restabelecimento da saude preciosa do Serenissimo Senhor D. João Principe do Brasil em Agosto d…: ode saphica. - Lisboa: na officina de Simão Thaddeo Ferreira*	*1789*	*without page*	*poetry*	*Impede ao Impio, ao Blasfemo immundo, Se atreva injusto, e cégo com demencia*
2	*Relaçam verdadeira da grande, e magnifica festividade com que no segundo dia de touros, que se conta… -: s.n.*	*1750?*	*6*	*poetry*	*Pois com firme demencia, Leve o fogo cruel da impassiencia Este carro hoje indigno sem demora*
3	*Villancicos que se cantaram na See do Illvstrissimo Senhor Dom Ioam de Mello Bispo Conde. Nas Matina… - Em Coimbra: na Officina de Manoel Rodrigves de Almeyda*	*1698*	*A5*	*poetry*	*Dormido el amor me aviza Que de mi culpa despierte Ay de mi si mi letargo Tanta demencia nò advierte*
4	*Amigavel dezengano aos peraltas: obra em verso / por seu indefectivel, e mais sincero amigo, Elio Prudencio Sileo, &c. &c. &c.. - Lisboa: na officina de Domingos Gonsalves*	*1784*	*11*	*poetry*	*Instigas-me, Illuzino? Tem paciencia; Que eu te vou declarar tua demencia*
5	*Sermam nas exequias do Excellmo, e Reverendmo Senhor D. Pedro de Alancastro… / pregov o o M. R. P. M. Fr. Iorge de Castro… no Convento da Arrabida… em 25. de Mayo de 1673. - Lisboa: na Officina de Ioam da Costa*	*1673*	*23*	*religion*	*que erro, que engano, que demencia, que doudice, querer começar a vida là despois dos annos, a que os mais pocos chegaõ, & estendem a vida?*
6	*Ensaio magico ou duas palavras sobre a feitiçaria. Em que se mostra a falsidade da arte magica, ou f… / por M. J. D. G. P. D. M.. - [Braga]: Typographia Bracharense*	*18--*	*4 16*	*religion*	*consiste a força da arte Magica nos enganos, e demencia nos enganados* *entre outras demencias affirmava que a feiticeira tinha poder para revocar os mortos*
7	*Naufragio, que passou Jorge Dalbuquerque Coelho, capitão, & governador de Paranambuco / [Antonio de Crasto]. - Em Lisboa: por Antonio Alvarez*	*1601*	*without page*	*poetry*	*Não tens Imperio algum, ne Magestade, Mas a mortal cigueyra, & a demencia Vencendo com Tulliana eloquencia, De modo que direy, tanta demencia*
8	*Comedia o Mais Heroico Segredo ou Artaxerxe: agora novamente traduzida, accrescentada, e disposta segundo o gosto do Theatro Portuguez, para se representar no Arrayal de Nossa Senhora do Cabo, nas festas do Cirio de Lisboa, anno de 1753 / composta na lingua italiana pelo abbade Pedro Metastasio. - Lisboa: na Officina junto a São Bento de Xabregas*	*1757*	*394*	*theatre*	*Bem haja a minha demencia pela qual me perdoais*
9	*Abecedario Real e Regia Instrucçam dos Principes Lusitanos, composto de 63. discursos Politicos, & M…: offerecido ao Serenissimo Principe Dom Joam N.S. / pelo M.R.P. Fr. Joam dos Prazeres, Prègador Gèral, & Chronista mòr da Religiaõ do Principe dos Patriarcas Sam Bento. - Lisboa: na Officina de Miguel Deslandes, Impressor de S. Magestade*	*1692*	*62*	*politics*	*E todo o Principe, que não souber usar de hum, & outro attributo, consoante a gravidade das culpas, & qualidade das pessoas, arrisca-se a cair na demencia*
10	*Index das cousas mais notáveis de que trataõ os seis tomos das Academias dos Humildes, e Ignorantes… - Lisboa: na Offic. de Ignacio Nogueira Xisto*	*1764*	*2 14*	*index*	*D. Affonso VI. Rey de Portugal sua demencia. 52. 411 Demencia. A do Rey D. Affonso VI. em huma pergunta. 43. 341*
11	*Epistolae ad Lucillium ;Epistolae Pauli et Senecae. - Paris: [Atelier du Soufflet Vert]*	*1475*	*15 77v.*	*philosophy*	*Nunc en quta demência est hominum turpissima vota diis insusurrt* *Nunc que demencia est supervacua discere tta tporis egestate que demencia est fugere cretro ire npossis*
12	*Arte de ingenio, tratado de la agudeza: en que se explican todos los modos, y diferencias de conceptos / por Lorenço Gracian. - Em Lisboa: na Officina, Craesbeeckiana*	*1659*	*110*	*philosophy*	*aquel aforismo de Seneca, que no ay Ingenio grãde que no tenga vn grano de demencia*
13	*Jubilos da América, na gloriosa exaltaçaõ, e promocaõ do Illustrissimo e Excellentissimo Senhor Gome…: collecção das Obras da Academia dos Selectos, que na Cidade do Rio de Janeiro se celebrou em obsequio, e applauso do dito Excellentissimo Heroe / pelo Doutor Manoel Tavares de Sequeira e Sá… Ex Ouvidor Geral da Comarca de Parnaguá [sic] no Estado do Brasil… - Lisboa: na Officina do Dor. Manoel Alvares Sollano*	*1754*		*panegyric*	*quem procederá a tal demencia, que queira delinquir até merecer a vossa ira, e reprovaçaõ*
14	*Nueva filosofia de la naturaleza del hombre, no conocida ni alcançada de los grandes filosofos antig… / composta por Doña Oliva Sabuco… - Impresso e[m] Braga: por Fructuoso Loure[n]ço de Basto*	*1622*		*philosophy*	*y por el tacto siente las otras cosas, y no a si mismo, como no siente, ni entiende su demencia, y locura* *no puede, el intelecto agens, componer razones perfetas, sino quales las veys en la demencia, y frenesi*
15	*Summa de la Theologia Moral: su materia, los tratados mas principales de casos de conciencia / su author el Reverendis. P. Fr. Jayme Corella… ; primera parte… - Em Coimbra: na Officina de Joam Antunes*	*1694*		*religion*	*Los niños, antes del uso de la razon, nò estan sugetos a las leys, ni tan poco los locos en el tiempo de la demencia* *Locos. En el tiempo que estàn con la demência, estàn escusados de la ley. pag.159. num.2*

16	*Descripção topografica, e historica da Cidade do Porto. Que contém a sua origem, situaçaõ, e antigui… / feita por Agostinho Rebello da Costa. - Porto: na Officina de Antonio Alvarez Ribeiro*	*1789*		*history*	*cada huma das Vogaes resolveo com sigo mesma, lançar o seu voto na Veneravel Berengaria, como por zombaria da confusa eleiçaõ, e naõ com animo sincero que recahisse nella similhante Cargo, pela sua incapacidade, e demencia*
17	*Diccionario poetico, para uso os que principião a exercitar-se na poesia portugueza: obra igualmente util ao orador principiante / seu author Candido Lusitano. - Lisboa: Of. Simão Thaddeo Ferreira.*	*1794*		*dictionary*	*demencia as synonym of the entries:* *Desatino* *Furor* *Insania* *Loucura*
18	*Retiro de cvidados, e vida de Carlos, e Rosaura: I. [-II.] Parte / composta pelo Padre Matheus Ribeyro, theologo, pregador deste Arcebispado, & natural de Lisboa ; dedicado a Christovam de Brito Lobo. - Lisboa: na Officina de Manoel Lopes Ferreira*	*1688*	*192*	*novel*	*He a demencia frenetico accidente da alma, disse Plutarco, he o amor ha especie de insania*
19	*Historia universal, em que se descrevem os imperios, monarchias, reynos & provincias do mundo, com m… / copiada de diversos authores, chronistas approvados, & authenticos geographos… pelo Padre Fr. Manoel dos Anjos… - Em Coimbra: na officina de Manoel Dias mercador de livros*	*1651* *1652*	*275*	*history*	*Instituio sua maldita secta contra a doutrina do velho, & novo Testamento. Acreceo a sua demencia a perfidia de Sergio Monge, em quem concorriam todas as maldades*
20	*Primeyra parte da Chronica de Cister: onde se contam as cousas principais desta religiam com muytas antiguidades, assi do Reyno de Portugal como de outros muytos da christandade / composta por Frey Bernardo de Brito… - Em Lisboa: por Pedro Crasbeek*	*1602*	*424*	*history*	*ha molher de nobre geração, & dotada de fermosura e riquezas, se lhe affeiçoou entranhavelmente, & chegava esta demencia a tanto, que não sintia quietação a hora que o não via*
21	*Compendio de orthografia, com sufficientes catalogos, e novas regras, para que em todas as Provincia…: accrescentado com outros novos Catalogos, e explicaçam de muitos Vocabulos antigos, e antiquados, para intelligencia dos antigos escritores portuguezes… / composto pelo R. P. M. Fr. Luis do Monte Carmelo… - Lisboa: na Officina de Antonio Rodrigues Galhardo*	*1767*	*260*	*grammar*	*Index entry: Demência, as. Vid. Tolo. § 10, Num. 7*
22	*Facta et dicta memorabilia / [coment.] Oliverius Arzignanensis. - Venezia: Guglielmo Anima Mia*	*1491*	*160v.*	*history*	*IDem cūm Atheniensium scelerata dementia tristem de capite eius sententiam tulisset*
23	*Despertador christiano eucharistico de varios sermones del Santissimo Sacramento del Altar…: Con una Epistola exhortatoria a los ministros evangelicos de la divina palabra / su autor… Don Joseph de Barcia y Zambrana… - Lisboa: en la oficina de Miguel Deslandes*	*1694*	*75*	*religion*	*Los Predicadores (dize) predicavam sus imaginaciones tan vanas como voluntarias: los Sacerdotes y superiores (lo que es màs lamentable) los aplaudian, y el pueblo gustava de sermones semejantes. O librenos Dios de tal demencia, dize San Agustin*
24	*Margarita poetica. - [Venezia: Giovanni Rosso]*	*1493*	*157v.*	*poetry*	*qui livore & īvidia cōmotus solita dementia in me psilvit*
25	*Do D. Monravá Novissima Medicina impugnante à nova, velha e velhissima dos autores antigos, e modern…: que dedica ao vigilante monarca D. Joaõ V… - Lisboa: na Officina do mesmo autor* *Vol. 3*	*1744*	*69* *90*	*medicine*	*In the chapter entitled Delirio:* *Porque huns a chamaõ Demencia, Crisis ou Apostema do Cerebro: outros Lesaõ do Entendimento, outros inflamaçaõ do Cerebro, outros inflamaçaõ das membranas delle; de sorte, que aquillo, que em outras membranas, he Erysipela, em as do Cerebro he Delirio* *Que os Precordios em nada contribuem, para as demencias, a cima tenho explicado. Nem a immerçaõ do Frenetico em agoa fria póde dar para elle idea de remedio*
26	*Vita Christi. - Milano: Giovanni Antonio di Onate para Pietro Antonio da Castiglione*	*1744*	*195*	*religion*	*nūc q demencia r suꝑuacua discere in tanta temporis egestate*
27	*Relaçaõ fiel e verdadeira das disputas, que huma mulher casada de fresco teve com seu marido pela na…: Obra muito util, e necessaria a todos utriusque sexus, que tiverem tentações de se casar, e àquelles, que já gemerem no cativeiro. - Lisboa: na Offic. Patr. de Francisco Luiz Ameno*	*1785*	*195*	*poetry*	*Que naõ era decente ao seu estado* *Que a senhora pozesse os pés na rua,* *Sem ser em Sége, fosse alhêa ou sua,* *Doutrina, que observou mui tenazmente,* *Tẽ que a morte a livrou de ser demente*
28	*Diccionario poetico, para uso os que principião a exercitar-se na poesia portugueza: obra igualmente util ao orador principiante / seu author Candido Lusitano. - Lisboa: Of. Simão Thaddeo Ferreira*	*1794*	*441* *479* *190* *68* *106* *409* *422* *439,440*	*dictionary*	*demente is synonym in the entries:* *imprudencia, impudencia, luxo, luxuria, vaidade,* *amor (lascivo), atheista, gastador, herege, impeto*
29	*Hexameron. - Augsburg: Johann Schüssler*	*1472*	*54v.*	*religion*	*Unde puto non avaricia nutriendi eum in dementē fieri*

30	*Epiphyllides in dialecticis.De Conversione propositionum secundum Peripateticos.Quaestio in Analytic… / Averroes ; [trad. lat.] Helias Hebraeus. – Venezia: Aldo Manuzio*	*1497*	*58*	*philosophy*	*quoddam dictum Alexandri, qđ ipse refert demente Theophrasti*
31	*Allegaçaõ de Direito, a favor de Domingos Ferreira de Abreu… na Causa crime, em que lhe he parte p… / por Jacintho da Sylva de Miranda… – Sevilha: En la Emprenta de los Herederos de Francisco de Leefdael*	*1751*	*52*	*law*	*Simulou tambem outra [procuração] em nome de seu irmaõ Demente para arrendar os fructos do seu Arcediagado de Evora*
32	*Compendio de orthographia, com sufficientes catalogos, e novas regras, para que em todas as Provincias…: accrescentado com outros novos Catalogos, e explicaçam de muitos Vocabulos antigos, e antiquados, para intelligencia dos antigos escritores portuguezes… / composto pelo R. P. M. Fr. Luis do Monte Carmelo… – Lisboa: na Officina de Antonio Rodrigues Galhardo*	*1767*	*111 and 112* *715*	*grammar*	*Tõlo, os. Este Nome se-entende ordinariamente por Mentecapto, e Demente, isto he, Homem, que carece de discurso por desordem da Fantasia, e Memoria corporal. Doudo, ou Doido, e Louco, he, quem carece ordinariamente de hum sério, e prudente discurso por nimia actividade ou precipitaçâm da Fantasia. Tonto he, quem carece de discurso, ao menos coherente, por debilidade da Fantasia, e Memoria corporal. Se a carencia de discurso coherente nasce de lesâm causada na Fantasia por enfermidade, o Tonto se-chama Delirante.* *Orátes. Sam doidos, lunaticos, dementes, &c*
33	*Introductiones ad commentaria legum criminalum, quae in libro quinto ordinationum Lusitaniae contine… / authore Joanne Thomas de Negreiros. – Ulyssipone: typis Regalibus Sylvianis, Regiaeque Academiae*	*1754*	*131* *54*	*law*	*servindo de Almoxarife da Casa dos Cincos, de que era proprietario Joseph do Rossignol, e pondo-se demente, e incapaz de poder servir o dito officio, sabendo o R. Nicolao Antonio Rossignol, seu pay, e outros parentes seus, que o Almoxarife se achava gravado com divida consideravel à fazenda Real, a fim de que esta naõ fosse satisfeita, pouco antes da sua morte, tiràraõ de sua casa muito movel precioso* *Distinguitur autem furiosus à demente; quia ille rabiem furoris signis exterioribus ostendit; hic verò mente caret, sed factis exterioribus furorem non indicat*
34	*Orationes et opuscula. – Venezia: Filippo Pinzi,*	*1496*	*78*	*various*	*Caeter neminẽ puto tã demente q oculis inflãmatis ipm audeat adhibere*
35	*Elegantiae linguae latinae ;De Pronomine sui.Lima quaedam Laurentii Vallensis / Antonius Mancinellus. – Venezia: Cristoforo de' Pensi*	*1496*	*24v.* *56v.*	*grammar*	*Nisi forte putamos dementẽ Scipionẽ africanũ fuisse* *& senes quidam dementes nunq resipiscunt*
36	*Opera / [coment. Antonius Mancinellus , Acron, Porphyrio e Cristophorus Landinus]. – Venezia: Boneto Locatello para Ottaviano Scoto*	*1494*	*260v.* *217v.* *114* *114v.* *59v.*	*various*	*Caetera qui vitae, hoc dicit in allis rebus illum nõ fuisse dementẽ* *Ac non ante malis dementẽ actũ furiis* *audiat inuidus Dementem strepitum lycus* *Dementẽ.i.furibũdũ & qualem ex nimia libidine hoĩes edunt* *dum capitolio Regina dementes ruinas Funus & imperio parabat*
37	*Institutiones oratoriae / [coment.] Raphael Regius. – Venezia: Boneto Locatello para Ottaviano Scoto*	*14[93]*	*117*	*rhetoric*	*Quare mihi tria haec verba vident ascribenda hoc dementẽ esse*
38	*Opera / [coment. Acron, Porphyrio e Cristophorus Landinus] ; [ed. Johannes Franciscus Philomusus]. – Venezia: Giorgio Arrivabene*	*1490/ 91*	*200*	*various*	*Acnõ aũ malis dementẽ actũ furiis*
39	*Opera philosophica ;Epistolae. – Venezia: Bernardino de' Cori e Simone da Lovere*	*1490*	*141v.* *70*	*philosophy*	*quẽ dementẽ alliga turus est* *Dementes hoc quod aliquando concupiscunt semper timent*
40	*Epistolae / [ed.] Johannes Andreae. – Roma: Arnold Pannartz*	*1476*	*5v.*	*religion*	*Nam ut inexpugnabilẽ sue ecclesiae dominus murum contra perfidos dementes q hereticos erigeret*
41	*De Priscorum proprietate verborum. – [Venezia]: Giovanni Rosso*	*1490*	*131* *102v.* *227v.* *181*	*dictionary*	*Exterminavit ut cõterminavit demente fecit Catul* *Regina dementes ruinas fumus & imperio parabat pro ipsa demens hyppallage est* *Quo niam neque mea nex nec intercessio posse ui detur aliorum dementem reprimere audaciam* *Chremes in medium in summũ ire ad dementes*
42	*Lexicon graeco latinum nouissime ab inumeris mendis recognitum, & insigni accessione auctum per Conr… – Basileae: ex officina Hieronymi Curionis*	*1545*	*without page*	*dictionary*	*entries from the Greek*

FIGURE 1. The Infante D. Afonso and a black pageboy (c. 1653), by Avelar Rebelo. Museu de Évora.

well have suffered from senile dementia *avant la lettre*. Unexpectedly, the *Veneravel Berengaria* assumed the mission as new Abbess, with the hallucinatory (?) support of the ghosts of the nuns buried in the convent.

The reference in [Table: 25] is a medical book, where *demência* is equated to delirium, and its pathogenesis linked to the inflammation of brain membranes. Very interestingly, a grammar dated 1767 advances an explanation of words that appears to harbinger present nosological distinctions [Table: 32]. *Demente* is the man who lacks thought and memory. *The Doudo, or Louco*, has no serious conversation due to excessive activity and rush of thought. The word *Tonto* is linked to frailty *(debilidade)*.

Finally, in the book [Table: 34] there is a chapter entitled *Galieni medici ad medicinam introductorium*, where treatment of ocular inflammation is considered, saying that only a *demente* would apply rose oil to the eyes.

The present work has strengths, namely the systematic nature of the search, taking advantage of a very large database of ancient books in Portugal.[12] It also has limitations, as the collection of books in *Biblioteca Nacional Digital* might be biased, and the search relied on automated word detection methods.

A final word, in spite having been established as a clinical concept, the word dementia has also been used in a literary vein by great Portuguese writers from the 19th century to the present, notably Almeida Garrett, Camilo Pessanha, Eça de Queiroz, Júlio Dinis, Fernando Pessoa, Ary dos Santos, and Herberto Hélder, as emphasised by Francisco Pinto.[13]

In conclusion, the term *demência* was found in the ancient Portuguese literature. Usually it was equivalent to madness, or departure from reason, but in some cases the meaning was quite close to the present clinical concept of dementia.

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HISTORICAL ARTICLE / MEDICAL LIBRARIES

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

Augusto e Jaime Celestino da Costa: Personal Libraries at Nova Medical School

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ABSTRACT: Augusto Celestino da Costa, a renowned histologist, and his son Jaime Celestino da Costa, a distinguished surgeon, represent two generations of prominent portuguese physicians. This study examines their personal libraries, which were donated to the Nova Medical School, Universidade Nova de Lisboa, and are now held with restricted access at the institution's library.

Using a mixed-methods analysis that integrates both quantitative and qualitative data derived from the bibliographic catalogue, we examined 1,884 volumes comprising 1,578 unique titles, primarily in the fields of Histology, Embryology, and Cardiothoracic Surgery. The works span from 1690 to 2009 and are written in Portuguese, French, English, and Spanish.

Our analysis provides insight into the professional interests and intellectual environments of both physicians, shedding light on the evolution of medical knowledge and education in Portugal. These collections also serve as valuable historical sources for understanding the development of medical sciences in the country.

KEY WORDS: Augusto Celestino da Costa; Jaime Celestino da Costa; Personal library; Medical library.

AUGUSTO CELESTINO DA COSTA

Augusto Pires Celestino da Costa (Figure 1) was born in Lisbon on April 16, 1884, into a family of Azorean descent. He was the son of Pedro Celestino da Costa (1852–1910), an infantry officer, and Maria Luísa Amélia Pires da Costa (?-1887). After his mother's death when he was three years old, his father married Joana Figueira de Magalhães, who became like a mother to Augusto. She was the niece of Carlos May Figueira, a physician of the Portuguese Royal House, who would become his first mentor [1].

He married Emília Hermengarda Croner, with whom he had four children: Pedro Celestino da Costa, Jaime Celestino da Costa, Elisa Celestino da Costa and Augusto Celestino da Costa. He graduated in Medicine at Escola Médico-Cirúr-

gica de Lisboa, in 1905. He dedicated himself to a medical career, university teaching, and scientific research, specializing in Histology. He was a pioneer in the study of Embryology and Histology in Portugal.

Augusto Celestino da Costa was admitted to the first technical histology course in 1901, organized by Marck Athias, and soon became his disciple.

Regarding his choice of Histology, Augusto explains that: *"I chose Histology due to a series of fortuitous circumstances: the extraordinary interest by reading about the neuron theory in Testut, the opportunity to find a mentor in Athias—whose name seemed to me to carry an invincible prestige when I saw it cited abroad [...]; and the fact that I had in my family the man who was the first to practice microscopy at our school [...] Professor May Figueira."* [2]

Augusto Celestino da Costa completed his medical degree with the dissertation *"Glândulas suprarenaes e suas homólogas: estudo cytologico"*[3], demonstrating his skills as a researcher by analysing the foundations of the duality of the adrenal cortex and medulla and studying the cells of each of these structures.

He was affiliated with several national and international institutions throughout his career. In Portugal, between 1901 and 1906, he worked at the Laboratório de Histologia Rilhafoles, at the Hospital Miguel Bombarda, at Laboratório de Histologia da Escola Médico-Cirúrgica, and at the Laboratório do Instituto Bacteriológico Câmara Pestana. Abroad, with financial support from his great-uncle May Figueira, he studied at the Anatomisch-Biologisches Institut in Berlin (Germany) between 1906 and 1907. In 1908, he trained at the Pathologisches Institut des Moabit-Krankenhaus and the Hygienisches Institut at the University of Berlin.

In 1917, he undertook further training in Madrid (Spain) at the Laboratorio de Investigaciones Biológicas. Between 1917 and 1922, he studied at the Institute of Embryology in Utrecht (Netherlands) and the Institute of Anatomy and Embryology in Brussels (Belgium).

In 1910, the year of the establishment of the Portuguese Republic and the death of Miguel Bombarda (responsible for the Histology and Embryology classes), Celestino da Costa, at the age of 27, was chosen to lead the Chair of Histology at the Faculdade de Medicina da Universidade de Lisboa (FMUL). There, he founded the Institute of Histology and Embryology, of which he was director.

In 1932 he was appointed as the delegate of full professors to the University Senate. In 1935, he was named director of the FMUL, a position he held until 1942.

As a specialist in Embryology and Histology, Augusto Celestino da Costa published 383 works, including textbooks on Embryology, Histology, and Histological Techniques. In his son words: *"Celestino da Costa approached his teaching mission with the same passion he dedicated to scientific work, with the same meticulousness in its execution, striving for completeness and lasting influence".*[4]

This commitment led him to write several textbooks to meet the needs of his disciplines. In this context, his first published didactic work was entitled *"Noções de Technica Histologica"*[5], followed shortly after by the *"Manual de Técnica Histológica"*[6], written in co-authorship with Pedro Roberto Chaves (1887–1951). His book *"Elementos de Embriologia"*[7] had several editions in Portuguese, Spanish, and French. In collaboration with Roberto Chaves, he also wrote the *"Manual de Histologia"*[8], which quickly sold out and was published in three volumes as part of the *"Tratado Elementar de Histologia e Anatomia Microscópica".*[9]

He established a research school in Portugal that advanced three fields: Cytology, Embryology, and Histology. However, Celestino da Costa was not just a researcher and a professor; he was also an enthusiast of several other subjects. In fact, between 1913 and 1921, he was the technical director of the Vasco da Gama Aquar-

Fig 1. Augusto Celestino da Costa, seated at his desk in his library.
Photograph from the personal archive of Augusto Celestino da Costa (NOVA Medical School library)

ium, which he sought to transform into a true marine biology institute. *"Celestino da Costa was a great researcher and professor of Histology and Embryology. But he was also a soul open to other scientific, spiritual, and human concerns. He was a true man of science, a cultured man in the broadest sense of the word, and a great and noble servant of Portuguese culture".* [10]

In 1929, the Junta de Educação Nacional (JEN) was established, and Augusto was elected vice president of what was the first generation of scientific agencies. In 1934, he assumed the presidency of the institution, a position he held for two years. In 1936, the institution was renamed Instituto para a Alta Cultura (IAC), and Augusto became its first president, a role he held until 1942.Born and raised in Lisbon, he was deeply interested in his city and its history, being elected president of the local group "*Amigos de Lisboa*". Augusto Celestino da Costa was a member of several national and international scientific societies. He was a founding member of the Sociedade das Ciências Naturais, the Archives Portugaises des Sciences Biologiques, the Sociedade Portuguesa de Biologia, the Sociedade Portuguesa de Endocrinologia, and the Sociedade Portuguesa de Anatomia. He also served as president of the Sociedade das Ciências Médicas de Lisboa. Celestino da Costa died at the age of 72 on March 26, 1956, in Lisbon, shortly after he presented a review paper on the embryology of the sympathetic nervous system[11] at the 43rd meeting of the Association des Anatomistes event (Figure 2).

JAIME CELESTINO DA COSTA

Jaime Celestino da Costa (Figure 3), son of Augusto Celestino da Costa, was born in Lisbon on September 16, 1915. Influenced by his father, he chose an academic, scientific, and professional career in Medicine.

Jaime was an important figure in Portuguese cardiothoracic surgery in the 20th century, being one of the founders and president of both the Sociedade Portuguesa de Cirurgia and the Sociedade Portuguesa de Cirurgia Cardiotorácica e Vascular.

According to Godinho, *"Professor Jaime Celestino da Costa was one of the most outstanding figures in 20th century Portuguese Medicine and Surgery. He belonged to a select group of individuals who stood out in our country for their intelligence, culture and outlook on problems. Endowed with great intelligence, a solid preparation, and vast culture, enlightened and well-travelled, lover of the arts in their various forms – literature, painting, music that he also performed – and still an expert in horsemanship - he was an excellent surgeon, a born organizer and a remarkable teacher".* [12]

After attending the Liceu Pedro Nunes (1925–1932), Jaime Celestino da Costa enrolled in the Faculdade de Medicina de Lisboa, established in 1911 at Campo de Santana and associated with the Hospital Escolar de Santa Marta. Jaime Celestino da Costa graduated in July 1938 during a period when his father was the director of the institution.

In 1940, he went to Paris to work as an intern at the Institut Curie, a private, non-profit foundation dedi-

Fig 2. Last photograph of Augusto Celestino da Costa.
Photograph from the personal archive of Augusto Celestino da Costa (NOVA Medical School library)

Fig 3. Jaime Celestino da Costa at the end of his medical course in 1938.
Photograph from the personal archive of Jaime Celestino da Costa (NOVA Medical School library)

cated primarily to oncological research, where he carried out an important part of his doctoral thesis.

In 1941, he began his academic career as an Assistant in Operative Medicine and Surgical Anatomy, and in 1944, he became Assistant of Professor Reynaldo dos Santos (1880–1970) in Pathology and Surgical Therapies. In 1945, at the age of 30, he completed his doctoral thesis at the Faculdade de Medicina de Lisboa, entitled *"A Parede Arterial"*. [13]

Jaime's professional career in Portugal began at the Hospitais Civis de Lisboa, where he became a surgeon in 1948 [14]. At the Hospital de Santa Marta, Jaime Celestino da Costa improved his surgical training with his mentor Reynaldo dos Santos. He also worked in the emergency department of the Hospitais Civis de Lisboa, gaining extraordinary experience as a surgeon.

In the same year he became an hospital surgeon (1948), cardiac surgery took its first steps, still with closed chest. At the Hospitais Civis de he performed his first cardiac surgeries: in 1951, a pericardial surgery; in 1953, mitral valve stenosis and patent ductus arteriosus. [12]

In 1958, he was transferred to Hospital de Santa Maria, where he became Director of the Department of Surgical Propedeutics. He created, in 1959, a Center for Cardiac Surgery within the Department, with the support of the Gulbenkian Foundation. There he prepared to perform open-heart surgery with hypothermia, which first took place in Portugal in the early 1960s. Extracorporeal circulation cardiac surgery began at the same time at Hospital de Santa Marta (which was then the core of the Serviço de Cirurgia Torácica of HCL) and at Hospital de Santa Maria. [15]

Jaime Celestino da Costa was also deeply concerned with hospital emergency care, writing on the topic, as exemplified by his work *"O problema da urgência na organização hospitalar"*[16], in 1959. He also presented and published the results of surgical training interventions: *"Ensino e treino cirúrgicos"*[17] and *"Uma experiência de ensino medico"*[18].

In 1972, he became clinical director at Hospital Santa Maria, and in 1973, he was appointed full professor of Surgical Pathology and director of the department. Finally, in 1979, he was responsible for the Department of Cardiothoracic Surgery. [12]

Jaime Celestino da Costa, while advocating for modern Medicine based on research and technical innovation, also believed in the concept of humanized Medicine, concerned with the doctor-patient relationship: "*Medicine is a profession that is both humanistic in nature and scientifically grounded. The humanistic aspect is the oldest tradition of clinical practice: it comes from the direct relationship between two personalities, the patient and the doctor.*" [16]

At international level, he was founding member of the European Society of Cardiovascular Surgery and an Honorary Member of the Society of Thoracic and Cardiovascular Surgery in Great Britain and Ireland. [14]

He retired on September 16, 1985, after 44 years dedicated to teaching at the Faculdade de Medicina da Universidade de Lisboa (FMUL). However, he continued to contribute to Portuguese Medicine through his publications, which include *"Formação dum cirurgião: um ensaio sobre ciência e arte"*[20], Um certo conceito da Medicina[19], and *"A geração médica de 1911: origem, realização e destino"*[21], essential works on the contemporary History of Medicine and Medical Education. He died on February 2, 2010, in Lisbon, at the age of 95.

METHODOLOGY

The initiative to study these collections arose from an activity conducted in 2023 at the library, which involved organizing an exhibition showcasing the early printed books held within the library's collections. At that time, it became apparent that the bibliographic holdings of these two collections possess a unique and historically significant value for the history of medicine in Portugal, warranting thorough study and dissemination.

To foster interest in the distinctiveness of these collections and their original owners, a case study was undertaken, utilizing the bibliographic catalogue of the FCM library. Accordingly, a biographical and bibliographical investigation of these two prominent figures in national medicine was conducted through comprehensive bibliographic and archival research, as well as an examination of their libraries based on content analysis, employing both qualitative and quantitative methodologies.

The biographical and bibliographical study of the owners of the libraries was primarily based on the analysis of the works contained within the library's collection. One of the main sources of information about Augusto Celestino da Costa was the work "*Augusto P. Celestino da Costa (1884–1956): A Crusade for Science*" by David-Ferreira and Tiago Brandão (2020). Equally important were the texts written by his son, Jaime Celestino da Costa, particularly those composed for the centenary celebration of his father's birth, as well as writings related to the Generation of 1911. These sources allowed for the con-

struction of a biographical portrait of Augusto Celestino da Costa's personal and professional life.

Regarding data collection, a report was exported from the library's catalogue, containing all the titles available in the personal library collections of Augusto and Jaime Celestino da Costa, which were donated to the FCM library. The report included the following information: registration number, document type, author, title, publication date, place of publication, publisher, subjects, language, country of publication, and notes mentioning dedications or other relevant information relating to each item.

For data processing, the report was exported to an Excel file, enabling the complementing of content analysis of the items in these collections using descriptive statistics and bibliometric techniques.

To present the results in a more structured and organized method, Excel was also used to create graphs and tables based on the collection's data.

Regarding the information collected about Jaime Celestino da Costa, it was primarily drawn from the book "*Um Certo Conceito de Medicina*", authored by Jaime himself, whose preface, written by João Lobo Antunes, identifies the work as an autobiography.

STUDY OF THE LIBRARIES OF AUGUSTO AND JAIME CELESTINO DA COSTA

"My father presented us with a dual image: the man in the laboratory, immersed in his scientific and research environment, and the cultured man, symbolizes in his library-office (the heart of our family life) where, with fictional works, we found also history books and many biographies [...]. The day I had to help fall apart that library, I felt like a plant cutting its own roots, destroying its own habitat". [18]

The personal libraries of Augusto and Jaime Celestino da Costa comprise a total of 1.884 volumes, with 1.578 unique records. Many of the works in Augusto Celestino da Costa's library were inherited from his great-uncle, the physician May Figueira (1829–1913), a distinguished figure in 19th-century Portuguese medicine (Figure 4).

Many monographs include dedications to both Augusto and Jaime Celestino da Costa, often from prominent contemporary authors, most of whom were colleagues in the medical profession of these two distinguished figures in Portuguese medicine.

According to Jaime, his father was always reading, even while walking on the street. In this regard, Jaime writes: *"How many times did we see him arrive home while reading on the street, bumping into lampposts, which he would avoid without interrupting his reading; once, still reading, he climbed a pile of sand placed on the sidewalk and descended again without even noticing it".* [18]

Jaime also mentions: *"Celestino's intellectual curiosity was unstoppable and revealed itself in his ability to read, to read constantly. I can see him arriving home for lunch, after stopping by the Barbosa tobacco shop on Rua do Carmo, with a bundle of newspapers under his arm [...] or any new book. He always carried a small paper knife in his pocket to open the next book. He would sit at the table and... read. Many times, he didn't even know what he had eaten or noticed the desolate look on my mother's face, who had stayed at the table just to keep him company. He read at the table as he read on the tram (his transportation), in the street, on the train, at the beach, or in the countryside. He read as a professional duty for information and rested by reading during breaks from work. [...] The books were not well cared for. He would bend their spines and damage them: like the reader, the book did not matter for its cover; it was the spiritual content that counted. In the vast library of thousands of books, all of them had been read, and even without a catalogue, their places were known. And if he didn't find a book right away, the agitation in that office was almost unbearable! My father's reading capacity was just one expression of his extraordinary work ethic".* [4]

Fig 4. Bookshelf with the collections from the libraries of Augusto and Jaime Celestino da Costa, at NOVA Medical School library.

PRESENTATION AND DISCUSSION OF RESULTS

Subjects – Thematically, 81% of the library's collection focuses on Medicine, while the remaining 19% encompasses other fields such as Biology, Literature, Botany, and Zoology, among others. In terms of medical specialties, the most prominent are Histology (307 titles), Embryology (190), Endocrinology (94), Anatomy (68), and General Surgery (60), as illustrated in Figure 5.

Beyond these specialties, the collection also includes a significant number of works on the History of Medicine (136 titles) and Medical Education (65).

Publication Dates – Although most of the work date from the 20th century, the collections include more than 350 works published before 1901. The most ancient book is from 1690: *"Correcçam de abusos introduzidos contra o verdadeiro methodo da medicina".* [22]

Countries and Languages – Regarding the languages of publication, as shown in Figure 6, there is a close balance between French (46%) and Portuguese (42%, both from Portugal and Brazil). There are works published in France, Belgium, and Switzerland.

Additionally, there are also works in English (8%), published in the United Kingdom and the United States, in Spanish (2%) from Spain, Argentina, Colombia, and Uruguay. Less represented are works in German (1%) and other languages, such as Italian and Latin (1%).

Authors – In addition to Augusto Celestino da Costa (345 works) and Jaime Celestino da Costa (92 works), the collections include works by important Portuguese authors, such as Luís Ernani Dias Amado (1901-1981) and Xavier Morato (1906-1989), each one of them with 29 works; Geraldes Barba (1917-1981) and Pedro Roberto Chaves (1887-1951), with 19 works; Luís R. Simões Raposo (1898-1934), with 14; J. Vasconcelos Frazão (n.d.), with 13; Reynaldo dos Santos (1880-1970), with 11 works; and Egas Moniz (1874-1955), with 10.

As far as foreign authors are concerned, we can mention Charles Robin (1821–1885), with 17 works; Claude Bernard (1813-1878), with 11; Charles-Polydore Forget (1800-1861) and René Leriche (1879-1955), each with nine; Santiago Ramón y Cajal (1852-1934), with seven; F. Xavier Bichat (1771-1802) and Gregorio Marañón (1887-1960), each with six; and Julian Huxley (1887-1975) and Pierre Flourens (1794-1867), each with five.

Personal Libraries as a Reflection of Their Owners – The personal libraries of Augusto and Jaime Celestino da Costa reflect their personalities; curious and deeply dedicated to Medicine and its History, as well as to science, particularly in the case of Augusto Celestino da Costa. Both Augusto and Jaime were not only physicians but also professors, a career they embraced with the same passion and commitment they had for Medicine.

Fig 5. Number of works in the collections by medical specialty.

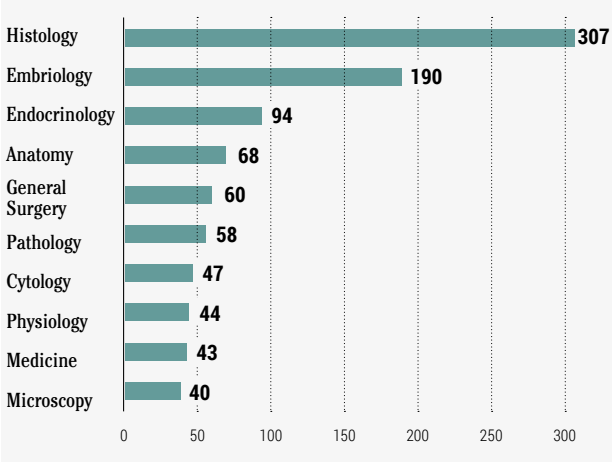
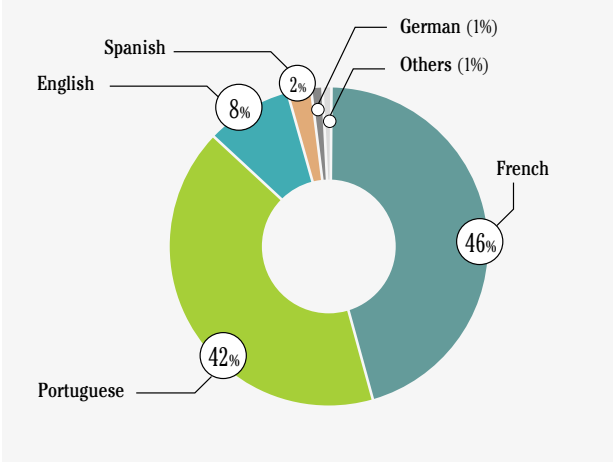


Fig 6. Percentage of works in the collections by language.



CONCLUSION

Personal libraries reflect the particularities and characteristics of their owners[23]. The libraries analysed in this study exemplify this idea: as medical libraries, they highlight the specialties to which both Augusto and Jaime dedicated themselves. However, they also include works on other medical subjects, and several topics ranging from Biology, Zoology or Pharmacology to Medical Education, on which both also wrote.

These collections are important sources of information both for and about the History of Medicine, in addition to providing insight into the period in which their owners lived, thus holding documentary value.

Augusto Celestino da Costa was a man of science, and the positions he held enabled him to write about his aspirations for science in Portugal, which, in his opinion, was behind other European countries. Jaime, on the other hand, distinguished himself for works on the History of Medicine and Medical Education, to which he dedicated himself mainly after his retirement. Both also wrote biographies of prominent contemporary figures, often as tributes and to keep alive the memory of those they admired and respected.

These are the libraries of two inquisitive physicians with a deep appreciation for reading and culture.

This study aimed to explore and publicize this collection so that it may serve as the subject of further research in the fields of Medical History and information science.

To conclude, a curious fact: the library of the NOVA Medical School located in Campo de Santana, specifically on Rua do Instituto Bacteriológico, houses these two collections, which are of great value for the study of the History of 20th-century Medicine. This location was formerly known as the Instituto Bacteriológico or Instituto Câmara Pestana, where Augusto and Jaime Celestino da Costa contributed to the advancement of medicine in Portugal. While the Instituto Bacteriológico once provided research opportunities, today these collections await further dissemination and recognition of their historical significance.

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JORNAL DA SOCIEDADE DAS CIÊNCIAS MÉDICAS DE LISBOA

Vascular Cognitive Impairment

Doctoral Thesis presented to the Faculdade de Medicina da Universidade de Lisboa. (March 2025)

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LESSON SUMMARY: Cognitive impairment of vascular cause, henceforth referred to as Vascular Cognitive Impairment (VCI), refers to any type of cognitive or behavioral impairment that results from cerebrovascular disease, regardless of its severity and impact on the person's functionality. Vascular Cognitive Impairment, as a broad concept, encompasses associations of other etiologies, including mixed etiologies. In its most severe form - Vascular Dementia (VaD), it implies a significant loss of function and behaves as a degenerative pathology which is therefore progressive. Vascular dementia is the second most common cause of dementia (after Alzheimer's disease), but its prevalence is uncertain. Although cognitive impairment caused exclusively by vascular pathology is uncommon, vascular pathology is often associated with other degenerative pathologies, especially with advancing age. Cognitive impairment resulting from the vascular component is often underdiagnosed, especially in its mild stage, as it is typically characterized by alterations in executive functioning, attention, processing speed, and less memory alterations. As it is a potentially preventable clinical entity, there is an urgent need to promote better knowledge of the disease and its identification. Cognitive assessment should be targeted at the defects mentioned, as the screening measures and global cognitive assessment commonly used (designed mainly with Alzheimer's disease in mind) may not be enough to detect them. Structural imaging tests are essential for diagnosis. There are no other biomarkers (apart from imaging) that can identify VCI in any of its stages, whether mild or more advanced. There are no approved therapies for the condition, and intervention should be aimed at vascular prevention and promoting better vascular health of the brain and better protection against injury.

KEY WORDS: Vascular Cognitive Impairment, Vascular Dementia, Cerebrovascular Disease, Cognitive Impairment, Executive Functioning, Vascular Pathology

Previous considerations

This lesson has not been designed for any particular audience. It is intended to be clear and simple to understand, but also thoughtful and cover the most recent and innovative aspects of the subject, including current research projects, so that it can inspire future lines of research.

This lesson could be adapted to integrate postgraduate training programs, for example in one of the PhD courses at the Faculty of Medicine of the University of Lisbon - the Neurosciences Doctoral Program or the Doctoral Program of the Academic Center of Medicine of Lisbon (CAML).

A comprehensive overview is given of the concept of Vascular Cognitive Impairment. Its evolution, the personal contributions and those of our working group to better understand the clinical condition and the diagnostic approach and intervention are highlighted. These contributions include participation in groups and in national and international studies, as well as the publications on the topic. In the field of research, Vascular Cognitive Impairment due to small cerebral vessel disease is covered in more detail, as it has been a major focus of our research.

CHAPTER 1
CONTEXTUALIZING THE CONCEPTS AND KNOWLEDGE OF PATHOLOGY

Conceptual evolution: from Dementia to Vascular Cognitive Impairment

Vascular dementia (VaD) has been known for several centuries, with historical accounts varying according to the sources[1]. It is possible that the first explicit reference was made by Jason Pratensis in the 16th century, in what is considered to be the first book dedicated to general neurology, *De Cerebri Morbis*[2], followed by Tomas Willis' descriptions in the 17th century, with the name *Dementia postapoplexya*. However, it truly became known just over a hundred years ago, when Otto Biswanger, Alois Alzheimer and Pierre Marie described, at the end of the 19th century and the beginning of the 20th century, patients with the clinical picture and neuropathological alterations characteristic of cerebral vascular pathology. Following these descriptions, Emil Kraepelin introduced the term *Arteriosclerotic dementia*. In 1894, during a conference in Dresden, Otto Biswanger described the macroscopic findings associated with a progressive clinical picture that he considered rare, distinct from that caused by syphilis, and called it *Encephalitis Subcorticalis Chronica Progressiva*[3,4]. It should be noted that, at this time, Biswanger described with particular emphasis the severe atrophy of the cerebral white matter, which in this form of the disease was mainly located in the occipital and temporal regions. The atrophy was associated with enlargement of the ventricular cavities, especially in the inferior and posterior horns. At the time, the frontal lobes seemed to be relatively spared, and the cortex had minimal involvement, so he justified his findings with a "diffuse nutritional" problem. The clinical picture consisted of progressive cognitive loss, with focal signs such as aphasia, visual alterations, unilateral motor or sensory defects. These focal signs fluctuated over time and co- existed with seizures. The condition began at the age of 50 and lasted at least 10 years, with periods of clinical stability[4,5]. At the same time, Otto Biswanger also described conditions resulting from atherosclerosis of large cerebral arteries - *Atherosclerotic Brain Degeneration*, and from embolic or thrombotic lesions of the arteries, which caused cerebral infarcts, calling them *Dementia Post Apoplexiam*, associated with acute lesions. In 1902, Alois Alzheimer used the term *Biswanger Disease* and histologically described the existence of neuronal loss, demyelination and sclerosis of the small perforating arteries of the cerebral white matter, with concomitant lesions in the white matter, internal capsule, lenticular nucleus, thalamus and protuberance, without alterations in the cerebral cortex[4]. Curiously, Alois Alzheimer already postulated the existence of an entity (in addition to those proposed by Biswanger) that he called *Senile Cortical Atrophy*, characterized by cortical small vessel disease, characterized by small wedge-shaped cortical infarcts, associated with gliosis and softening of some circumvolutions, which became severely atrophic and with indentations in the cortex[4]. At the time, he admitted the existence of mixed cases in its etiopathogenesis, as well as describing cases with very typical characteristics[4,6]. It should be noted that Pierre Marie had described *État criblé* in 1901, corresponding to the disease of small perforating vessels[5]. It should be noted that it was only much later, in 1974, that Hachinski introduced the term *multi-infarct dementia*[7], despite the concept already being subliminally understood beforehand.

As can be understood from the brief description above, which is not without controversy, cognitive impairment caused by cerebral vascular disease has been accepted as a clinical entity distinct from Alzheimer's disease for over a hundred years, and its histopathological characteristics were already well known[8].

In recent decades, evidence has emerged to support the broader concept of cognitive impairment of vascular cause (henceforth referred to as Vascular Cognitive Impairment - VCI), which encompasses any type of cognitive impairment, regardless of the severity of the cognitive condition, resulting from cerebral vascular disease, ranging from cognitive impairment without criteria of dementia (Mild Cognitive Impairment of Vascular etiology - MCIVasc) to impairment with functional and autonomy impairment (Vascular Dementia - VaD, or major neurocognitive disorder of vascular etiology, depending on the criteria used)[9-14]. On the other hand, the concept of cognitive impairment of vascular etiology encompasses the whole spectrum of vascular pathology (in the diversity of cerebral vascular pathologies) to vascular contributions in other cognitive pathologies, often referred to as "mixed etiologies", i.e. in concomitance with other degenerative pathologies. This entity is considerably more useful clinically than the "traditional" VaD and allows for the identification of patients at a time of mild pathology, and where, from a theoretical point of view, a preventative intervention effort is possible. On the other hand, the identification of cerebral vascular pathology in other pathologies (particularly common in Alzheimer's disease, but let's not forget other etiologies such as Lewy body disease) [15,16] allows for better prevention even in the case of other degenerative diseases[17].

Therefore, the investigation of a patient with cognitive impairment should always be an opportunity to detect concomitant vascular pathology and an opportunity for better prevention. For this reason, in a joint European initiative, and under the auspices of the *European Stroke Organization* (ESO), I was able to lead a recent publication with suggestions for a very practical approach, dedicated to identifying and guiding the diagnosis of cerebral vascular pathology in patients being investigated for cognitive complaints[18].

Diagnosis and diagnostic criteria

Vascular Cognitive Impairment is a very heterogeneous entity, both in its clinical manifestations and in the diversity of cerebral vascular lesions that can cause it, which includes the location of the lesion/lesions and their severity, and the form of onset (from the acute to the more chronic form).

Turning now to vascular dementia, it is important to remember that dementia syndrome implies a loss of cognitive abilities (reflecting a clear decline from a previous level), and this loss has repercussions on professional, family or social life, with a corresponding loss of autonomy[9,10].

To make a diagnosis of VD or major neurocognitive disorder due to cerebrovascular disease, it is necessary to have dementia syndrome (with a characteristic cognitive profile), imaging evidence of cerebrovascular disease, and a possible association between the observed cerebrovascular pathology and the clinical picture, in addition to excluding other causes of dementia[9, 10].

For more than 30 years, there have been various criteria, which I will refer to as "classic" VaD, which have tried to encompass the three aspects mentioned[9,10,19,20]. The classic clinical criteria for VaD have several limitations. One of the biggest limitations of these more traditional criteria was the neuropsychological model used, often influenced by the Alzheimer's disease model in which memory deficits predominate[9,10]. Another limitation came from the definition of vascular pathology and its relationship with cognitive impairment, which was often limited to a temporal relationship, which did not include more chronic forms of damage, such as small cerebral disease. An effort was made to make the criteria more adapted to the pathology. However, there were still limitations, particularly in terms of their ability to identify cases, i.e. their specificity and their sensitivity. The criteria of the *Alzheimer's Disease Diagnostic and Treatment Centers* (ADDTC)[20] take up the historic Haschinski scale (*Hachinski Ischemia Score*)[1] [21] and adapt the neuropsychological profile, no longer making memory impairment mandatory. In the criteria of the *National Institute of Neurological Disorders and Stroke* (NINDS) and the *Association Internationale pour la Recherche et l'Enseignement en Neurosciences* (AIREN) - NINDS-AIREN, although the profile should include alterations more typical of vascular disease, the memory impairment remained mandatory[19]. Both the ADDTC and NINDS-AIREN criteria include the possibility of a possible or probable diagnosis and the definition of

1 The Hachinski scale was originally developed to help differentiate between multi-infarct dementia and Alzheimer's disease and has become a useful clinical and research tool.

the necessary neuroimaging. Some of the studies that evaluated the clinicopathological correlation and compared the diagnostic identification capacity between these different criteria found a low probability of a patient being simultaneously identified by the various criteria, i.e. low reproducibility[22-24]. In addition, half of the patients who met the neuropathological criteria for Vascular Dementia did not have a clinical diagnosis of Vascular Dementia because they did not meet the diagnostic criteria, particularly regarding the temporal relationship between the clinical picture and the vascular lesion[25,26]. The evolution of the concept of Vascular Cognitive Impairment went hand in hand with the evolution of the diagnostic criteria proposed for cognitive impairment due to cerebrovascular disease, which, although not overlapping and still not consensual, very broadly designate the same entity. Various criteria have been proposed[12,13,27,28]. Recently, an international group of experts, in which we participated, drew up a consensus on this definition[12,28]. This consensus, like others based on the opinions of experts in the field, has made a clear effort to define the cognitive condition and the underlying vascular pathology, but it still lacks clinical validation in prospective studies and lacks neuropathological validation[12,13,27,28].

Trying to address the prevalence

In general, Vascular Dementia is the second most frequent cause of dementia and is generally attributed to around 20% of dementia cases[13]. The prevalence is highly dependent on studies, varying between 8 and 15% in the community, and between 0.03 and 58% in anatomopathological studies[29] with an incidence rate varying between 0.42 and 2.86%, increasing with age, and doubling in prevalence every 5.3 years after the age of 65[30,31]. The epidemiological data on cognitive impairment caused by vascular pathology is particularly difficult to interpret, due to all the aspects mentioned above, in addition to the difficulty in capturing the prevalence of cerebrovascular disease as a contributor to cognitive impairment with a mixed etiology[32]. Although it is very common with ageing, especially when co-existing with other pathologies[30], cerebrovascular pathology in isolation (or so-called "pure", without any other mark of degeneration) is not very common as an etiology of cognitive impairment, especially in the brains of older people. For this reason, there is enormous variability in the data available, depending on the methodologies used[33,34]. It is therefore possible that estimates of cognitive impairment caused exclusively by vascular pathology do not reflect the magnitude of the impact of vascular pathology on cognitive impairment in general, and dementia in particular. In our country, the prevalence study using the methodology of the "10/66 Dementia Research Group"[35] estimated the prevalence of dementia in the community at 9.23% (95% CI 7.8-10.9)[36], a much higher figure than would be obtained using the *Diagnostic and Statistical Manual of Mental Disorders-IV* (DSM) classification[9]. The estimated proportion of cases of vascular dementia was 16.3% (including 10.9% of "pure" cases and 5.4% of "mixed" cases with associated Alzheimer's disease). However, it should be noted that in 30.2% of the cases identified as "dementia" by the 10/66 DRG algorithm, we were unable to assign a specific subtype diagnosis. Despite the few studies in our country[35,37,38], the predominant impact of vascular risk factors on patients with cognitive impairment has recently been emphasized[37]. Internationally, depending on the type of studies and the criteria, prevalences of between 4.5% and 48.5% are found for isolated vascular disease in clinical studies, the highest in Japan for small vessel disease over the age of 65[39]. In anatomopathologically confirmed studies, the variability is also marked, with an average of 11% (ranging from 8 to 35%) of pure vascular disease in neuropathological studies[29], and concomitant disease with other degenerative pathology between 10 and 12%[40], making up to 25% of the vascular contribution from a neuropathological point of view[41]. In the *Rush Memory and Aging Project*, a longitudinal study with neuropathological assessment, Schneider and colleagues found a vascular contribution in 54% of the patients who developed dementia, with only 12% having isolated vascular pathology[33]. Also in neuropathological studies, in a 30-year retrospective study, Brunnström and colleagues found that vascular dementia existed in 23.7% of patients, while the combined etiology of vascular disease and Alzheimer's disease was reported in 21.6% of patients[40].

CHAPTER 2
CLINICAL ASPECTS OF VASCULAR COGNITIVE IMPAIRMENT

Vascular Cognitive Impairment can present phenotypically in different ways, which is due, on the one hand, to the diversity of vascular etiologies and the heterogeneity of the lesions, and on the other hand, to the

way in which these vascular pathologies can manifest themselves (abrupt or progressive).

Annex 1 summarizes the possible etiologies of Vascular Cognitive Impairment. When cognitive impairment occurs after a stroke, the impairment may be immediate (in the case of lesions in strategic areas)[42] or it may appear progressively after the stroke and is referred to as post-stroke cognitive impairment. Vascular lesions can be of different types, ischemic or hemorrhagic, single or recurrent. They can correspond to situations such as venous thrombosis or subarachnoid hemorrhage, arise because of vascular events in a post-traumatic context, be the consequence of small perforating vessel disease, or even compromise cerebral circulation and oxygenation secondary to systemic pathology or genetically determined diseases.

The difficulty created by these various clinical conditions, and the multiplicity of aspects linked to them, led to a European initiative with the production of a document with a practical clinical approach, in which the cognitive profile in patients with cerebral vascular disease was emphasized, as well as suggestions for guiding these patients[43].

In this lesson, we will look in more detail at the clinical aspects of Vascular Cognitive Impairment due to small vessel disease, as it is the most common form of the disease and the one to which our research group has been most dedicated. Post-stroke cognitive impairment is also addressed, as it is the next most common form of VCI and represents a good example for understanding the underlying mechanism.

The clinical presentation

When there are no focal signs resulting from vascular lesions, or a clear previous cerebrovascular episode (as is the case with VCI due to small vessel disease), the vascular cognitive impairment can be particularly difficult to identify. In the early stages of the disease, symptoms are dependent on the involvement of cognitive domains such as mental processing speed, attentional capacities and executive functioning, with difficulty in tasks mediated by programming and planning, as well as a reduction in initiative, affecting memory-related processes to a lesser extent, as is the case in Alzheimer's disease[44-46]. It should be noted that the involvement of memory does not exclude the possibility of diagnosis[44]. Since it can develop very slowly, the condition may not be noticed until the advanced stages of disability, and in the early stages it can be mistaken for the ageing process itself. It should be noted that these patients typically have no subjective complaints[46], which can make it even more difficult to suspect the diagnosis. In the LADIS (*Leukoaraiosis and Disability*) study[2], we found that the participants included in the first assessment who had subjective memory complaints (and who were completely autonomous in activities of daily living) performed worse in the neuropsychological assessment, especially in memory measures (even if they were within normal parameters)[47]. In these same participants, there was no correlation between these complaints (and their neuropsychological assessment) with the severity of cerebrovascular lesions[47]. Over time, we found that these same participants with memory complaints had, after three years, an increased risk of progressing to Alzheimer's disease and not to Vascular Dementia[48]. The vascular cognitive condition can often be attributed to other co-morbidities, such as depression. This aspect seemed particularly important to us, and we have shown that depressive symptoms can themselves be a hallmark of vascular pathology[49] and are associated with an increased risk of cognitive impairment. In the LADIS study, we confirmed that, in patients with evidence of cerebral small vessel disease, depressive symptoms were associated with an increased risk of cognitive decline and progression to dementia after three years of follow-up[50]. For this reason, the study of a patient with suspected VCI must necessarily include an assessment of neuropsychiatric symptoms[43].

It's not surprising, given all the aspects mentioned, that the global measures of cognition usually used may not be sensitive to identifying these cognitive conditions[43]. The *Mini Mental State Examination* (MMSE)[51], although a very useful and well-known instrument, may represent a particular limitation, as it focuses mainly on memory and language. The *Montreal Cognitive Assessment* (MoCA)[52], which includes items designed to assess functions other than memory and language, would be additionally useful. However, the fact that it is highly dependent on the level of education and literacy requires that the results be carefully integrated into the clinical context. For these various reasons, patients suspected of having VCI should un-

2 The LADIS (Leukoaraiosis and Disability) study, European multicenter study in which we participated, with European funding, sought to investigate the impact of age-related vascular changes in the white matter (one of the manifestations of cerebral small vessel disease) on disability over time. Our group was responsible for standardizing and coordinating the cognitive component throughout the study.

dergo formal neuropsychological assessment, whenever it is accessible and feasible. The neuropsychological assessment must include an evaluation of the cognitive domains most affected[43]. In the LADIS study, we developed a neuropsychological battery specifically designed for this type of patient[53], which was developed with the particularity that it could be implemented in several European countries, and whose validity we confirmed through a confirmatory factor analysis[54], and which was used on the participants in the LADIS study throughout the three years of follow-up. Over the last two decades, various batteries for assessing Vascular Cognitive Impairment have emerged, and in the work already mentioned, in the context of the *European Stroke Organization*[43], we made a very practical application suggestion based on the experience of various European groups in this field. However, it is important to point out that, in the absence of access to formal neuropsychological assessment, global cognition assessment measures continue to be used. As we showed in the LADIS study, the global measures of cognition used in that study were important predictors of dementia after three years of follow-up in people with evidence of changes in small vessel disease[55]. Additionally, and in the group of Portuguese participants included in our center, we showed that the MMSE was the most useful instrument for predicting dementia after 10 years of follow-up[56].

The identification of the clinical picture is therefore highly dependent on the existing suspicion and knowledge of the disease, on the one hand, and on the other, the sensitivity of the clinician approaching the patient. The interview should be detailed, gathering additional information on non-cognitive alterations. There is currently some evidence that the neuroimaging findings of small vessel disease are associated with a range of clinical manifestations, suggesting a phenotype of multi-system involvement, a field that is certainly yet to be explored[57]. Among the symptoms most classically associated with Vascular Cognitive Impairment caused by cerebral small vessel disease, non-cognitive motor symptoms are frequent[58], with gait changes[59] (usually short strides), frequent falls and increased lower limb tone, hypophonia, dysphagia and altered fine movements[58]. Another frequent symptom is urinary control dysfunction. In the LADIS study, we showed how participants with severe cerebral small vessel pathology, at a time when they were still autonomous, without significant cognitive decline, had complaints about urinary control, particularly urinary urgency[60]. Recently, in a systematic review, our group showed that moderate to severe alterations of cerebral white matter are associated with complaints of overactive bladder and incontinence with urinary urgency[61, 62], and a detailed evaluation of these complaints is currently under investigation.[3]

Imaging assessment

Neuroimaging is fundamental to the diagnosis of VCI. Structural imaging lesions consist of sub-cortical or cortical ischemic lesions of different sizes, hemorrhagic lesions, changes due to small vessel disease - such as cerebral white matter changes, lacunae or microhemorrhages. Some aspects are more specific to certain etiologies, such as cortical microhemorrhages and superficial cortical siderosis, for example, which are particularly associated with cerebral amyloid angiopathy. In the LADIS study, we showed how moderate to severe cerebral white matter changes (considering the Fazekas visual scale, which defines three severities - mild, moderate and severe)[63] and lacunes[64], considering their location particularly in the subcortical gray matter, were associated with worse cognitive performance[65], both in global cognitive measures[66] and in measures of mental processing speed, attention and executive functioning in autonomous people with evidence of cerebral small vessel disease[65]. In these patients, atrophy co-exists, even cortical atrophy, with subcortical atrophy being more characteristic. We also found that corpus callosum atrophy was associated with cognitive decline and a decline in motor skills over time[67]. It is possible that corpus callosum atrophy is a mechanism involved in the decrease in psychomotor speed, as it is associated with altered communication of inter-hemispheric information between homologous cortical areas[68]. In view of our findings, we also believe that there is a synergistic effect between cortical atrophy and the severity of white matter alterations, which determines cognitive deterioration in these patients[69]. Atrophy can be diffuse or focal after localized vascular lesions[43]. However, brain atrophy profiles with more focal characteristics should lead to the suspicion of other neurodegenerative diseases, such as atrophy of the internal temporal lobes in Alzheimer's disease or fron-

3 PhD project underway at CAML entitled Age-Related White Matter Changes and Lower Urinary Tract Dysfunction - One Step Towards OverActive Bladder Phenotyping (OSTOAP Study), doctoral student: Dr. Ricardo Pereira da Silva.

totemporal atrophy in frontotemporal lobar degeneration[43].

The most sensitive structural test for identifying cerebral vascular pathology is brain magnetic resonance imaging (MRI). If this is not possible, computerized axial tomography (TC) is clinically useful. When magnetic resonance imaging is performed, the appropriate sequences for identifying vascular pathology must be included. Annex

2 provides a schematic presentation of the information that can be provided by each sequence, which is commented on below. In addition to the 3D T1 and T2 sequences, the FLAIR (*Fluid Attenuated Inversion Recovery*) sequence should be performed to detect small cortical infarcts and accurately assess changes in the cerebral white matter, and also the SWI (*Susceptibility-Weighted Imaging*) sequence or Gradient Echo or T2* to detect microhemorrhages, superficial cortical siderosis (both of which are again usually missed on CT) and even old macrohemorrhages. Finally, the diffusion sequence (DWI - Diffusion-Weighted Imaging) is essential for detecting acute lesions, especially if they are small[43]. In the LADIS study, the alterations found in the diffusion sequences, in apparently normal brain tissue in the other sequences, were associated with a faster decline in cognitive processing speed, executive functions and working memory, as well as greater functional incapacity and increased mortality[70]. More recently, and with a view to research in the context of clinical trials, we took part in drawing up a guiding document for the use of cognitive instruments in clinical trials, particularly designed for small vessel disease and based on the literature published in this area, called Structure for Clinical Trials in Small Vessel Brain Diseases (FINESSE)[4][71]. Following on from this initiative, and in line with previous work, the use of additional sequences is suggested, namely the Diffusion Tensor sequence (DTI, encompassing fractional anisotropy - FA and mean diffusivity - MD), which allows subtle losses of tissue microstructural integrity to be assessed in regions where conventional MRI sequences are normal[57]. These losses of microstructural integrity correlate with cognitive ability, which could make it possible to identify patients with very early disease and, as such, those who can be better and more effectively intervened in clinical trials[73, 72].

MRI is also better at distinguishing other pathologies such as inflammatory demyelinating lesions, vasculitis, infectious, metabolic (ionic), toxic processes, and changes more typical of some genetic vascular pathologies (such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy - CADASIL, and adult leukodystrophies).[43]

The lesion pattern of the vascular disease can also guide the diagnosis. A high lesion load of white matter changes, lacunes and microhemorrhages in the basal ganglia suggests the effect of vascular risk factors, particularly hypertension. Severe cerebral white matter disease with extension to the temporal lobe, associated with lacunes, in younger patients suggests a monogenic disease (such as the afore mentioned CADASIL). Multiple cortical infarcts, especially in multiple cortical territories, suggest a cardioembolic source. Subcortical and basal ganglia microhemorrhages are typical of arterial hypertension, while their lobar location at the cortico-subcortical junction is more indicative of cerebral amyloid angiopathy, especially if associated with superficial cortical siderosis[43].

Implications for the identification of cerebral small vessel disease

The prognosis of cerebral small vessel disease, which is manifested by the clinical picture described above, which is indolent and slow, can be very unfavorable[74]. The LADIS study has shed more light on the impact of small vessel disease on cognition and the transition from a state of health to a state of dependence.[5] In this same study, we found that severe white matter alterations were associated with worse cognitive performance in global cognitive functions, executive functions, attention and motor speed[65]. In a 3-year follow-up of this same population, we confirmed that severe white matter changes were a poor prognostic factor for cognitive decline over time, tripling the risk of progressing to dementia after three years[73]. In this population, *de novo* lacunes[76] and worsening global atrophy[77] were also associated with progression to cognitive impairment. Erkinjuntti proposed specific research criteria for subcortical ischemic vascular disease[78]. Using Erkinjuntti's criteria[78,79], we found that small vessel disease was associated with poorer performance in cognitive processing speed, attentional abili-

4 The Framework for Clinical Trials in Small Vessel Brain Diseases (FINESSE) was created under the aegis of the International Society of Vascular Behavioral and Cognitive Disorders.

5 The participants in the LADIS study cohort, aged over 65, were autonomous and had no significant cognitive defects when they were included in the study.

ties and executive functioning, as well as poorer verbal fluency[80]. Over the three years of follow-up, an acceleration of decline was observed, especially in mental processing speed and cognitive functioning, as well as in global measures of cognition[81].

Cognitive impairment after acute vascular injury

The study of cognitive impairment secondary to acute cerebral vascular injury, which is the second most frequent cause of cognitive impairment due to vascular pathology, is a good model for highlighting the vascular mechanism as a cause of cognitive impairment and is not only limited to strategic infarcts.

The recognition of cognitive impairment after acute vascular lesions has been complemented in recent years by the identification of an increased risk of cognitive impairment even after transient lesions (Transient Ischemic Attack - TIA), underlining the role of vascular disease as a phenomenon that goes beyond the scope of focal lesions[82].

In the case of cognitive impairment following acute vascular injury, it should be borne in mind that isolated sequelae (such as aphasia) can imply functional impairment even without being sufficient criteria for dementia and can remain relatively static over time.

On the other hand, the sequelae defects (e.g. motor, sensory, visual) of a vascular injury can make it difficult to perceive the existence of a functional defect secondary to cognitive decline and can make it more difficult to identify. In addition, depressive symptoms are common after a stroke[83]. In a prospective study of stroke survivors, we showed how the presence of these same symptoms can already indicate an evolution towards cognitive impairment[83].

Acute vascular injury produces damage to a specific area of the brain, with focal signs and symptoms associated with that damaged area. Additionally, in the hyperacute phase (a concept closely associated with reperfusion therapies, and which covers the first few hours after the stroke)[84], there is a process that some authors call *transient cognitive impairment*, for which a possible inflammatory or cholinergic etiology is postulated, reactive to the acute vascular injury[85,86]. This transient condition seems to be distinct from confusional syndrome or *delirium*, a well-known condition in the acute context of stroke, which our work group described more than two decades ago[87]. Although it still lacks a definition of its own, *transient cognitive impairment* is broader in its symptomatic expression, not only reflecting the manifestation of the focal lesion area, and its prognostic value is still unclear[85,86]. After the acute phase, the focal vascular lesion can be associated with cognitive deterioration with two different evolutions. These developments may reflect two different mechanisms, which is why they will be briefly discussed below. On the one hand, a progressive deterioration over time after the acute vascular event, which may represent a form of anticipation of degenerative dementia due to the stroke. This mechanism has been epidemiologically supported by the fact that the risk of a dementia diagnosis doubles in stroke survivors compared to people who have not had a stroke[82]. These diagnoses of dementia shortly after a stroke (even if they don't involve a strategic area for cognition) share characteristics with Alzheimer's disease, and the presence of the APOE ε4 genotype has been identified as a factor that increases the risk of post-stroke cognitive impairment, as well as the presence of brain and temporal lobe atrophy[82,88-90]. On the other hand, there is a distinct evolution, characterized by an initial phase of recovery from the vascular lesion, with stabilization for some time, followed by a later decline, which is more frequent in patients with recurrence or multiple stroke locations. Levine and colleagues found in a sample of 23,572 participants (515 of whom had had a stroke) how stroke was associated with cognitive loss associated with the acute event, but above all with deterioration over the years after the stroke, both in global measures and in executive functioning, and how this evolution was different from people who had not had a stroke[81]. The same type of trajectory was described in a sample based on nine longitudinal hospital cohorts from seven different countries, published by Jessica Lo and colleagues[92] in 2022, finding that in 1,488 stroke survivors (from an initial sample of 2,295) followed over time there was an initial period of improvement in the first year after the stroke, followed by a decline in global cognition, with the most marked progression being associated with stroke recurrence and advanced age. Several studies have investigated whether amyloid pathology could be the determining factor in post- stroke cognitive decline, having carried out positron emission tomography (PET) with radiopharmaceuticals labeling the amyloid peptide in stroke survivors. In these studies, they found that most of these stroke survivors who developed dementia in the years after the stroke did not have amyloid uptake suggestive of concomitant Alzheimer's

disease[93-95]. Using advanced magnetic resonance imaging methods, Duering and colleagues found aspects compatible with remote neurodegeneration after subcortical vascular lesions, causing a focal reduction in cortical thickness and loss of white matter[96], with a poorly understood mechanism, possibly due to an inflammatory reaction[97] or synaptic damage[98]. This phenomenon has been understood as a process of distant disconnection and has been investigated[99]. Some studies carried out on experimental animals (which are clearly outside the scope of this lesson) have sought to replicate this same mechanism[100]. Finally, there is no evidence to support that vascular pathology is a trigger for the formation of amyloid plaques, despite the frequent co-existence of the two pathologies, especially with advancing age[101].

While the degenerative phenomenon that occurs in many stroke survivors remains unexplained, the existence of partial or temporary reversibility that is observed in patients with cognitive impairment of vascular cause is well accepted, and an additional motivation for identifying this entity with the aim of intervening. Unlike the typical fluctuations of Lewy body disease, which oscillate around a progressive deterioration plan, and contrary to the usually progressive and continuous evolution of Alzheimer's disease, patients with vascular pathology do have a possibility of reversibility when the lesion is in the context of an acute stroke[102], or even in a systemic vascular context[103].

CHAPTER 3
PREVENTION AND TREATMENT

Risk and protective factors

In recent decades, observational epidemiological studies have suggested that vascular risk factors contribute to cognitive decline and dementia, not only for VCI, but also in Alzheimer's disease[104]. Livingston and colleagues had previously found that up to 40% of dementia cases could be attributed to potentially modifiable factors, most of which were vascular risk factors[105]. Recently, in the update of this same document produced by the *Lancet Commission*, the addition of two more risk factors to the twelve previously identified led the authors to conclude that up to 45.3% of dementias could be attributed to risk factors, most of which were vascular and modifiable[106]. Several studies have been carried out, in populations at high vascular risk and with combined intervention strategies in various areas[107-110]. However, evidence that modifying these factors actually translates into dementia prevention has been more difficult to obtain[111,112], with promising results, but not yet sufficient to produce robust recommendations[113]. The difficulty in generating this evidence has led to the recent proposal by the FINESSE group (mentioned above) to consider more selected populations, with very early vascular disease and characteristic and specific profiles in future clinical trials[71]. Again citing the LADIS study, we found that hypertension, diabetes and stroke were associated with worse cognitive performance - particularly in executive functions, attention and mental processing speed, in autonomous people with evidence of cerebral small vessel disease[65], and among these risk factors, diabetes remained an independent factor predicting cognitive decline and dementia over time[75], an effect that is not unrelated to the already known association between diabetes and cerebral amyloid deposition[114].

Several factors have been identified as protective of cognitive decline. In the LADIS study, we confirmed that a low level of education is associated with a higher risk of cognitive decline[50]. On the other hand, participation in leisure activities, both physical and cognitive, plays a preventive role in the incidence and progression of dementia[106, 115]. The recent *Lancet Commission* review reinforces the importance of cognitive reserve and staying socially active as protective factors against developing dementia of any etiology[106]. Several studies have suggested that physical activity can delay or prevent the functional decline associated with ageing and promote overall health. In the European observational study LADIS, physical activity was found to be associated with better cognitive performance among autonomous people[116] and also as a factor associated with less progression to cognitive impairment of any etiology and particularly to Vascular Dementia[117]. Recently, in a systematic review, we showed that physical activity has a protective role, particularly in cognitive impairment and vascular dementia[118], but these results were based only on observational studies. In this context, we carried out the AFIVASC study[6]. The AFIVASC study aimed to assess the impact of a six-month physical activity intervention on people diagnosed with vascular mild cognitive impairment in

6 AFIVASC stands for "Physical Activity and Vascular Cognitive Impairment", a randomized study funded by FCT[2014]. The AFIVASC study was approved by the Ethics Committee of Hospital Santa Maria and Hospital Santo António do Porto. AFIVASC was registered on ClinicalTrials.gov (NCT03578614).

terms of their cognitive performance, quality of life, functional status and physical function[119]. The inclusion criteria consisted of having a diagnosis of vascular mild cognitive impairment[13], being fluent in reading and writing in Portuguese, with no relevant functional alterations. The exclusion criteria were contraindication (due to medical or orthopedic pathology) to physical activity. In this population, we showed how physical activity, even before randomization and active intervention, was associated with better ability to perform cognitive tests[120]. We found that participants were unable to accurately assess their own physical capacity subjectively, compared to a standard of objective measures (use of accelerometry)[120]. It is worth noting that, in general, physical activity has been described as safe in people with cognitive decline and dementia[118]. The AFIVASC study showed an improvement in the physical capacity of the participants and showed how it was possible and safe to carry out a randomized study with physical activity in patients with Vascular Cognitive Impairment. Although the main objective of the study was not achieved, a *post-hoc* analysis showed cognitive improvement in participants who met the World Health Organization's recommendations for physical activity, measured objectively[121].

Therapeutics

There is currently no specific therapy for Vascular Cognitive Impairment. Therapy for Vascular Cognitive Impairment largely involves general health promotion measures, optimizing the correction of vascular risk factors and stroke prevention[122]. In stroke patients, the recommended secondary prevention measures should be implemented[43]. Treatment should always be individualized, depending on the underlying cerebrovascular disease. In all cases, control of hypertension, hypercholesterolemia and smoking, as well as measures to reduce obesity and treat diabetes should be considered, as these factors are associated with an increased risk of cardio-cerebrovascular diseases in general. Contrary to what happens in the secondary prevention of ischemic stroke, there is no evidence that antithrombotic or anticoagulant therapy is effective in preventing the progression of VCI[123]. Although there is no evidence that patients with "pure" VaD benefit from drugs approved for symptomatic therapy of Alzheimer's disease, the frequent co-existence of vascular pathology with amyloid-type degenerative pathology could lead to their use for symptomatic benefit[18,124].

The lack of specific therapeutic measures for cognitive impairment due to vascular pathology led our group to try an intervention mediated by physical activity, which has already been mentioned[120,121], but also an intervention directly aimed at cognitive rehabilitation specifically for patients with Vascular Cognitive Impairment. Together with the Faculty of Sciences of the University of Lisbon, we developed a *software program* centered on a common activity - shopping in a supermarket, which was aimed at training attention skills, processing speed and action planning and programming[125-128]. While can be done autonomously in mild stages of the disease, it will require help in more advanced stages and is aimed at everyday activities[127].

In a simplified outline, the approach to these patients should always include: 1. Identifying vascular risk factors; 2. Optimizing therapy for vascular risk factors, with a special focus on hypertension, diabetes, lipid profile, vascular events, control of systemic pathologies that may compromise correct cerebral oxygenation (e.g. heart failure, obstructive sleep apnea syndrome); 3. Advising on a healthy lifestyle, including regular physical activity and preventing social isolation; 4. Promoting cognitive activities and monitoring cognitive complaints that can be corrected (e.g. reduced initiative, attention training) in individuals with vascular risk factors, taking special care in individuals with a combination of several risk factors; 5. Assessing the impact of symptoms on the person's life, using non-pharmacological interventions applicable to other cognitive pathologies, including support for the caregiver, depending on the person's specific needs. We refer to two recent recommendations produced in a European context and in which we participated, which are a useful tool in the management of these patients[124,129].

CHAPTER 4
FUTURE PROSPECTS FOR RESEARCH INTO VASCULAR COGNITIVE DEFECTS

Despite the advances in knowledge of Vascular Cognitive Defect, many aspects remain to be clarified. These include the identification of biomarkers, particularly accessible serum markers, and advanced imaging techniques for earlier identification. In the field of genetics, considerable progress has been made in recent years, with the identification of various monogenic forms of cerebral small vessel disease[130-132]. The fact that these pathologies share clinical and neuroim-

aging characteristics with sporadic forms has helped to improve our understanding of the pathogenesis of small vessel disease and to identify potential therapeutic targets[132]. The identification of several genes associated with a higher risk of developing the disease can also identify high-risk individuals who will also be good therapeutic targets[71]. Some recent studies have addressed the application of drug-genomic tests[7] and there are already published trials with drugs commonly used in clinical practice for the prevention of vascular events associated with cerebral small vessel disease[133,134].

There is also a need for better knowledge of the determinants of the different sub-types of Vascular Cognitive Defect. For example, data linking cholesterol levels throughout life and the risk of developing dementia has been controversial. Very recently, a longitudinal study showed that low serum HDL (high-density lipoprotein) cholesterol values were associated with an increased risk of subcortical vascular dementia, due to damage to small cerebral vessels, but not Alzheimer's disease or dementia with mixed characteristics[135]. Progress in clarifying the particularities of the subtypes of Vascular Cognitive Defect could be decisive in deciding on therapeutic targets. Finally, there is some data suggesting that regression of vascular lesions of the cerebral white matter is possible, particularly in patients who do not have alterations in the microstructural integrity of the white matter [136], with a controversial mechanism that remains unexplained. The possibility of regression further promotes the need to invest in prevention, which should cover the interaction between risk factors and protective factors at different stages of life. Recently, an open clinical trial showed a potential benefit of drugs with potential effects as vascular endothelium stabilizers in cognitive impairment caused by lacunar vascular events, but the results of a more robust design are still awaited[137].

Our work group is continuing its research aimed at better understanding the clinical expression of the disease and trying to modify its evolution. In this sense, the study OSTOAP (*Age-Related White Matter Changes and Lower Urinary Tract Dysfunction - One Step Towards OverActive Bladder Phenotyping*) aims to assess the relationship between small vessel disease and urinary function, with a clinical aspect that includes an exhaustive neuro- and urological assessment, and a more fundamental research aspect, with research into potential biomarkers in blood, urine and cerebrospinal fluid.

Another of our group's lines of research deals with the impact of physical activity on vascular cognitive impairment. The results of the AFIVASC randomized study[121], already commented on, instigate a need to reflect on the implementation of clinical trials with physical activity, and make it urgent to improve the available evidence on the relationship between physical activity and cognitive ability, including the assessment of adherence to physical activity itself. Notably, there is a lack of information on how the brain of elderly individuals with cerebrovascular disease responds to exercise. In this context, we feel the need to add better evidence on this topic, and it is in this context that our future research is situated.

Following the articles published in recent years, studies on prevention and adherence to preventive measures are expanding and will certainly be, in the absence of curative drugs, a viable way of changing health parameters, particularly in cognitive health and cognitive impairment caused by vascular pathology.

7 Pharmacogenomic tests (also known as pharmacogenetics) are part of precision medicine technologies and make it possible to assess the specific response of each individual and their genetic profile to the metabolism of a given drug.) The field is expanding rapidly and can target a single or several genes simultaneously and evaluate the response to a drug or combinations of drugs.

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ANNEX 1

Etiologies of Vascular Cognitive Impairment

- Disease of the small cerebral vessels due to arteriosclerosis of the small caliber arteries (penetrating or perforating arteries), referred to as lipo-hyalinosis. It manifests as white matter changes, lacunae and micro-hemorrhages (typically deep).
- Infarcts (cortical, cortico-subcortical, single or multiple, of different sizes) resulting from pathology in larger caliber arteries.
- Strategically located infarcts (e.g. in the angular circumvolution, in the territory of the posterior cerebral artery, in the territory of the anterior cerebral artery, in the thalamus).
- Hypoxia/anoxia/hemodynamic effect.
- Hemorrhagic vascular accidents, including subarachnoid hemorrhage.
- Cerebral venous thrombosis.
- Cerebral amyloid angiopathy.
- Congenital/genetically determined pathology that can lead to multiple vascular lesions of different types (coagulation disorders, metabolic diseases).
- Monogenic vascular diseases (such as CADASIL).

ANNEX 2

Schematic representation of the information that each MRI sequence can provide.

The following table was taken from the article Verdelho et al, 2021 ESJ; and as such kept in the original version[1].

Table 2. MRI sequences in CI due to CVD should include

Sequence	Provides information on:
T1-weighted	brain morphology, focal or diffuse atrophy
T2-weighted or fluid-attenuated inversion recovery (FLAIR)	white-matter hyperintensities, old vascular lesions
Diffusion-weighted imaging (DWI)	number, size and location of most recent ischemic lesions
Susceptibility-weighted imaging (SWI)/GRE-T2*	microbleeds, cortical superficial siderosis

1. Verdelho, A., Wardlaw, J., Pavlovic, A., Pantoni, L., Godefroy, O., Duering, M., Charidimou, A., Chabriat, H., & Biessels, G. J.[2021]. Cognitive impairment in patients with cerebrovascular disease: A white paper from the links between stroke ESO Dementia Committee. European stroke journal, 6[1], 5-17.

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