30_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI, PER N. 4 POSTI DI RICERCATORE SANITARIO, CATEGORIA D LIVELLO D SUPER, DA ASSEGNARE ALLA SC NEUROLOGIA 9 – MALATTIE CEREBROVASCOLARI

PROVA I

1. Aspetti patofisiologici della angiopatia amiloide cerebrale: similitudini e differenze con la malattia di Alzheimer

2. A cosa serve il programma Microsoft Excel?
   a) realizzare fogli elettronici per analisi di dati
   b) realizzare presentazioni
   c) gestire spool di stampa

3. Leggere e tradurre

Vascular Remodeling in Moyamoya Angiopathy: From Peripheral Blood Mononuclear Cells to Endothelial Cells

The pathophysiological mechanisms of Moyamoya angiopathy (MA), which is a rare cerebrovascular condition characterized by recurrent ischemic/hemorrhagic strokes, are still largely unknown. An imbalance of vasculogenic/angiogenic mechanisms has been proposed as one possible disease aspect. Circulating endothelial progenitor cells (cEPCs) have been hypothesized to contribute to vascular remodeling of MA, but it remains unclear whether they might be considered a disease effect or have a role in disease pathogenesis. The aim of the present study was to provide a morphological, phenotypical, and functional characterization of the cEPCs from MA patients to uncover their role in the disease pathophysiology. cEPCs were identified from whole blood as CD45dimCD34+CD133+ mononuclear cells. Morphological, biochemical, and functional assays were performed to characterize cEPCs. A significant reduced level of cEPCs was found in blood samples collected from a homogeneous group of adult (mean age 46.86 ± 11.7; 86.36% females), Caucasian, non-operated MA patients with respect to healthy donors (HD; $p = 0.032$). Since no difference in cEPC characteristics and functionality was observed between MA patients and HD, a defective recruitment mechanism could be involved in the disease pathophysiology. Collectively, our results suggest that cEPC level more than endothelial progenitor cell (EPC) functionality seems to be a potential marker of MA. The validation of our results on a larger population and the correlation with clinical data as well as the use of more complex cellular model could help our understanding of EPC role in MA pathophysiology.

PROVA ESTRATTA

13/03/2026

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PROVA 2

1. Correlazione tra genotipo e fenotipo nel CADASIL

2. Per URL si intende una sequenza di caratteri che:
   a) identifica univocamente l'indirizzo di una risorsa web
   b) un componente del sistema operativo
   c) un linguaggio di programmazione

3. Leggere e tradurre

Understanding the Pathophysiology of Cerebral Amyloid Angiopathy

Cerebral amyloid angiopathy (CAA), one of the main types of cerebral small vessel disease, is a major cause of spontaneous intracerebral haemorrhage and an important contributor to cognitive decline in elderly patients. Despite the number of experimental in vitro studies and animal models, the pathophysiology of CAA is still largely unknown. Although several pathogenic mechanisms including an unbalance between production and clearance of amyloid beta (Aβ) protein as well as 'the prion hypothesis' have been invoked as possible disease triggers, they do not explain completely the disease pathogenesis. This incomplete disease knowledge limits the implementation of treatments able to prevent or halt the clinical progression. The continuous increase of CAA patients makes imperative the development of suitable experimental in vitro or animal models to identify disease biomarkers and new pharmacological treatments that could be administered in the early disease stages to prevent irreversible changes and disease progression.

PROVA NON ESTRATTA

13/03/2024

Matteo Poli

30_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI, PER N. 4 POSTI DI RICERCATORE SANITARIO, CATEGORIA D LIVELLO D SUPER, DA ASSEGNARE ALLA SC NEUROLOGIA 9 – MALATTIE CEREBROVASCOLARI

PROVA 3

1. Il ruolo dell'angiogenesi nella malattia di Moyamoya: causa o effetto?

2. Il termine "Open Source" indica:
   a) un software i cui autori ne permettono e favoriscono il libero studio e l'apporto di modifiche da parte di altri programmatori
   b) un software che può essere modificato da chiunque a patto di corrispondere all'autore una offerta libera
   c) un software protetto da diritti d'autore che non può essere modificato da nessuno tranne da chi ne detiene i diritti

3. Leggere e tradurre

Three-tiered EGFr domain risk stratification for individualized NOTCH3-small vessel disease prediction

Cysteine-altering missense variants (NOTCH3cys) in one of the 34 epidermal growth-factor-like repeat (EGFr) domains of the NOTCH3 protein are the cause of NOTCH3-associated small vessel disease (NOTCH3-SVD). NOTCH3-SVD is highly variable, ranging from cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) at the severe end of the spectrum to non-penetrance. The strongest known NOTCH3-SVD modifier is NOTCH3cys variant position: NOTCH3cys variants located in EGFr domains 1–6 are associated with a more severe phenotype than NOTCH3cys variants located in EGFr domains 7–34. The objective of this study was to further improve NOTCH3-SVD genotype-based risk prediction by using relative differences in NOTCH3cys variant frequencies between large CADASIL and population cohorts as a starting point.
Scientific CADASIL literature, cohorts and population databases were queried for NOTCH3cys variants. For each EGFr domain, the relative difference in NOTCH3cys variant frequency (NVFOR) was calculated using genotypes of 2574 CADASIL patients and 1647 individuals from population databases. Based on NVFOR cut-off values, EGFr domains were classified as either low (LR-EGFr), medium (MR-EGFr) or high risk (HR-EGFr). The clinical relevance of this new three-tiered EGFr risk classification was cross-sectionally validated by comparing SVD imaging markers and clinical outcomes between EGFr risk categories using a genotype-phenotype data set of 434 CADASIL patients and 1003 NOTCH3cys positive community-dwelling individuals.
CADASIL patients and community-dwelling individuals harboured 379 unique NOTCH3cys variants. Nine EGFr domains were classified as an HR-EGFr, which included EGFr domains 1–6, but additionally also EGFr domains 8, 11 and 26. Ten EGFr domains were classified as MR-EGFr and 11 as LR-EGFr. In the population genotype–phenotype data set, HR-EGFr individuals had the highest risk of stroke [odds ratio (OR) = 10.81, 95% confidence interval (CI): 5.46–21.37], followed by MR-EGFr individuals (OR = 1.81, 95% CI: 0.84–3.88) and LR-EGFr individuals (OR = 1 [reference]). MR-EGFr individuals had a significantly higher normalized white matter hyperintensity volume (nWMHv; P = 0.005) and peak width of skeletonized mean diffusivity (PSMD; P = 0.035) than LR-EGFr individuals.

PROVA NON ESTRATTA

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