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Meeting Abstracts

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Virtual Conference Abstracts

The Risk of Polypharmacy and Potentially Inappropriate Drugs in Residential Care Dementia Patients: Tips from the Phare Study

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Abstract

Aims: The aims of the present study, conducted in two regions of Italy, Calabria and Piedmont, were: to assess the use of inappropriate drugs according to the Beers Criteria; to study the possible drug-drug interactions; to perform the possible strategies for avoiding the potential harmful prescriptions, by using the STOPP and START criteria.

Methods: Data were obtained retrospectively from 972 residential care patients between 2016 and 2018.

Results: Mean age was 82.4 ± 8.4 years old, with a prevalence of women (64.8%). ADL, IADL, MMSE, CIRS, NPI and number and kind of drugs were recorded. A classification of potential inappropriate drugs was made according to the Beers criteria. Data were collected through an Excel file able to gather the main information. In the case of suspected adverse event, Naranjo Scale was applied. The study of possible drug-drug interactions was made by Micromedex 2.0. Functional and cognitive impairments, comorbidities and number of drugs were assessed. The bivariate relationship between number of drugs and Modification of Diet in Renal Disease (MDRD) showed that the higher the number of drugs used was, the worst was kidney function assessed ($p = 0.0001$). The most frequent inappropriate drugs were anticholinergic drugs, tricyclics antidepressants, long half-life benzodiazepines, antipsychotics and proton pump inhibitors.

Conclusions: These data are very interesting and show the need for an accurate choice of drugs in elderly people and for starting a wise deprescribing procedure.

A Clinical Case of a Patient Carrying a Rare Pathological PSEN1 Gene Mutation (L424V) Demonstrating the Phenotypic Heterogeneity of Early Onset Familial AD

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Abstract

We present a clinical case of an EOAD patient carrying a rare form of the PSEN-1 mutation with onset of cognitive decline and initial behavioural symptoms. His clinical presentation exemplifies the symptomatic variability of EOAD in its aetiologically clarified monogenic forms.

This 39-year-old gentleman initially presented with gradual behavioural changes. Relevant medical and family history, investigations, including MRI brain, all confirmed a working diagnosis of a dementia syndrome.

Early onset familial AD was accepted as a primary diagnosis and a complete blood sample for genetic testing was obtained. Whole exome sequence (WES) analysis for 21 targeted genes associated with an array of inheritable neurodegenerative disorders was performed, which identified a heterozygous missense variant Leu424Val in PSEN-1 gene judged to be likely pathogenic, and to our knowledge, only been reported once until now.

Comparing our results with a reported Spanish case, identical polymorphism associated with two profoundly distinct phenotypic presentations was seen, along with a difference in neuroimaging findings, and the presence and absence of seizures in the Spanish and Bulgarian case, respectively.

Comparing the phenotypic expressions of Leu424Val (g.71074C > G) with other PSEN-1 mutations, showed it as an "atypical" PSEN-1 polymorphism. Age of onset could also be determined by looking at the data of other mutations in the same codon.

Our study confirms that in EOAD with positive family history, high-throughput sequencing can be especially informative. In our view, WES should be considered as a first-line examination in detecting EOAD given its practicality, ease of sample collection and affordability.

Keywords

Early-onset, PSEN-1 mutation, Genetic polymorphism, Whole exome sequencing

The Multisystemic Origins of Alzheimer's disease

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Abstract

In 2003 I established the company Mimex Montague Healthcare Limited to commercialise the Strannik technology developed by Dr Igor Gennadyevich Grakov. By 2006 I had realized that he had developed a mathematical model of the relationship between sense perception by brain function, the autonomic nervous system and physiological systems, and cellular and molecular biology; and had applied this in his Strannik software to screen and treat patients.

Around 2010-15 this became the subject of the EC's Human Brain Project i.e. to create such a model and to use it to screen the pathological correlates of complex conditions such as Alzheimer's Disease. Moreover, in recent years eminent Alzheimer researchers and co-workers have spoken of the need to understand the systems which regulate the body's function and to use such knowledge to screen and treat Alzheimer's patients.

So, it is my intention to speak about the fundamental mechanism by which the brain regulates the stable and coherent function of the body's physiological systems; to demonstrate how the Strannik software does so; and then to discuss how this technology can be used to screen and treat the Alzheimer patient.

Exploring the Effect of Diabetes on Brain Structure and Perfusion in Patients with Early Alzheimer's Disease

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Abstract

Background: Alzheimer's disease (AD) can have a significant detrimental effect on the cerebrovascular system. Type II diabetes mellitus (T2DM), along with being a risk factor for AD, can affect cerebral blood flow. Comorbid T2DM in AD could cause additional cerebrovascular burden that may result in further damage to brain structure and function than that which is seen in AD.

Methods: The current study compares 48 patients across the AD spectrum with and without T2DM (with 24 patients in each group). Voxel based morphometry was used to determine volumetric differences in grey matter using T1-weighted magnetic resonance images and tract based spatial statistics was used to examine differences in white matter integrity. To assess whether these structural differences were associated with a reduction in cerebral blood flow, arterial spin labelling was used to measure cerebral perfusion.

Results: Patients with T2DM showed lower cerebral perfusion in brain regions that showed lower brain structure. These brain regions were the caudate nucleus, the cingulum bundle and the cerebellum. These differences were restricted to the right hemisphere.

Conclusions: Microvascular and macrovascular complications could contribute toward the negative effects on brain structure seen in AD patients with T2DM. Furthermore, the right lateralised effects seen in the present study could arise due to the characteristic trajectory of the arteries supplying the brain. The additional burden resulting from comorbid T2DM and AD could accelerate disease progression. Therefore, the modifiable nature of cardiovascular risk factors could offer an avenue for intervention to help mitigate the rate of disease severity.

Time-Varying Functional Connectivity Fading Analysis and Classification of Alzheimer's Disease, Mild Cognitive Impairment and Normal Control Subjects based on Resting-State fMRI Data

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Abstract

In this talk, we will explore the fading effect in time-varying functional connectivity of AD, MCI and NC subjects based on the resting-state fMRI data, and see how that can be exploited for more accurate AD, MCI, NC classification. The research was motivated by the fading effect in wireless communications, where severe channel fading is related to information loss during the transmission. We show that in some critical brain regions, compared with NC subjects, AD patients suffer more severe and long-lasting fading in the functional connectivity level; in other words, AD patients show selective loss in the amount of information successfully exchanged between the brain regions. On the other hand, MCI subjects experience less severe and shorter fading in functional connectivity level in general, and the connectivity level of MCI may be tangled together with that of either NC or AD. We also show that comparing with static network connectivity pattern analysis that extracts only the region-level spatial variability, dynamic network connectivity pattern analysis, which exploits both the temporal and spatial variability in functional connectivity, can achieve much higher accuracy in the classification of AD, MCI and NC. When the AD, MCI and NC subjects are all mixed together, the prediction accuracy of time-varying connectivity-based classification is 90.9%, 75.0% and 80.0% for NC, MCI and AD, respectively. Our result is consistent with existing results on dynamic functional connectivity analysis for AD and MCI.

The Promise of Clinician-Delivered Cognitive Training for Mild Cognitive Impairment (MCI)

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Abstract

Cognitive training delivered face to face by a clinician has the potential to slow the progression of cognitive decline in patients with mild cognitive impairment (MCI) and subjective cognitive decline (SCD). We examined this potential in two studies using an intense, metronome-paced multicomponent cognitive training intervention originally created for children designed to remediate multiple cognitive skills including working memory, long-term memory, processing speed, fluid reasoning, visual and auditory processing, and attention. In the first study, we compared two methods of delivering 80 hours of training to 292 participants ranging in age from 51 to 95 with subjective memory or attention complaints. Both delivery methods resulted in significant gains across all cognitive skills, as well as transfer to improvements in mood, memory, cognitive efficiency, life application skills, and attention. In the second study, we examined cognitive training as part of a Functional Medicine intervention with physical exercise, anti-inflammatory diet and nutritional supplements, sleep optimization, and stress management for five cognitively impaired patients over age 50. Following the intervention, three of the five patients were no longer classified as cognitively impaired, a fourth patient improved to only mildly impaired, and the most severely impaired patient remained steady. Patients reported improved memory, mental clarity, and outlook on life. fMRI analyses revealed changes in brain connectivity and efficiency. Both studies support the potential of face-to-face cognitive training for MCI and SCD in patients over age 50 as a standalone intervention or as part of a holistic approach to slowing cognitive decline in this population.

Mechanistic Deconvolution of Alzheimer's Disease from Pre- and Co-Morbidities

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Abstract

Although genetic factors have a modest effect on Alzheimer's risk, the vast majority of cases are considered to be non-familial, and no clear recipe exists for determining genetic predisposition. Stronger arguments may instead be made for the role of prior health and medical history. Specifically, a variety of infectious diseases, plus autoimmune and metabolic disorders such as diabetes, hypertension, obesity, Crohn's disease, COPD, macular degeneration and glaucoma are all statistically significant individual predictors of an eventual Alzheimer's diagnosis, and specific combinations tend to amplify the predictive power.

While prior literature has argued that such peripheral pre- and co-morbidities tend to amplify Alzheimer's risk via the simple, non-specific factor of systemic inflammation, recent advances in Alzheimer's biomarkers suggest a specific, logical etiology is at play- one that elucidates novel targets for both early-stage prophylaxis and mid- to late-stage therapeutic intervention, with the crucial factor relating to anomalous protein post-translational modifications that manifest broadly in both co-morbidities and Alzheimer's disease itself.

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