16th Annual Meeting of the International College of Geriatric Psychoneuropharmacology &
5th International Congress on Psychiatry and the Neurosciences

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Book of Abstracts

Co-sponsoring Organisations:

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Welcome Message

It is a special pleasure to welcome psychiatrists, neurologists, pharmacologists, basic neuroscientists, social and behavioral scientists as well as any professional involved in neuropsychiatric research and/or clinical care to the joint congress event consisting of the 16th Annual Meeting of Geriatric Psychoneuropharmacology and the 5th International Congress on Psychiatry and the Neurosciences. These congresses are organized jointly by the International College of Geriatric Psychoneuropharmacology (ICGP) and the Hellenic Society for the Advancement of Psychiatry and Related Sciences (HSAPRS); moreover, they are being co-sponsored by the World Psychiatric Association (WPA), the World Federation of Societies of Biological Psychiatry (WFSBP), the International Neuropsychiatric Association (INA) and the Hellenic Psychogeriatric Association (HPA). Having been honored through the active engagement of these respectable international scientific organizations, our main aim is to promote the interface and interaction among various disciplines as they relate to Neuropsychiatry and Geriatric Psychoneuropharmacology. As ambitious as it might be, our effort in implementing the integrated congress program is to seek for any convergence of all relevant disciplines in quest of constructive synthesis, which could eventually lead to the betterment of research outcome and clinical care in Neuropsychiatry and Geriatric Psychiatry.

In the present Congress, the many prominent scientists who feature as our guest speakers and who will share with us their knowledge and experience are the best guarantee towards a successful outcome. We are proud indeed to see that the final program includes: (a) two keynote lectures, one by Sir Robin Murray titled “At last we have a model of schizophrenia that integrates social and biological phenomena”, and one by Professor Alan Thomas on the “Neurobiology of late-life depression”; (b) seven plenary lectures to be given by distinguished speakers; (c) approximately twenty symposia, organized by prominent scientists under the auspices of ICGP and HSAPRS; (d) six symposia independently organized by WPA, INA, HPA, as well as the Eating Disorders Section of the Hellenic Psychiatric Association; and (e) three seminars organized by WPA and HPA, as well as a special session for young investigators, by ICGP.

The high scientific caliber of all congress sessions will guarantee a most informative scientific event, offering an excellent platform for interaction among leading clinicians and researchers with an interest in geriatric psychiatry and areas of general psychiatry related to the neurosciences. Moreover, it is the organizers’ aspiration to provide an opportunity for senior scientists to impart knowledge and wisdom to junior researchers and physicians in need of guidance and mentorship.

Last but not least, the hosts shall spare no effort in making your participation scientifically rewarding and meaningful and your stay in Athens as enjoyable as possible. Thus, we are confident that you will carry back home pleasant memories of this occasion.

Constantin Soldatos  
HSAPRS President

Angel Moriñigo  
ICGP President
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It is widely acknowledged that late-life depression is a complex phenomenon. Its boundaries with normality are contested and diagnostic criteria disputed. However, in spite of such concerns much progress has been made in identifying biological substrates for depression in older people. Advances in neuroimaging (both structural and functional) have led to a wide range and large number of investigations which have reported many abnormalities. These have identified both likely underlying substrates in the brain for depression (neural circuits) and mechanistic processes which appear to impact on these circuits to induce depressive symptoms and syndromes. Neuropsychological studies report a range of deficits, predominantly in information processing, executive and memory functions, whilst other reports identify genetic, immunological, vascular, metabolic, morphological, neurochemical, neuroendocrine and assorted other biological changes. Overall we are faced with a bewildering number of reports of biological abnormalities in late-life depression covering a wide range of investigative techniques and areas. This lecture will attempt to summarise and synthesise these, identifying the most robust and consistent findings and putting these findings into several inter-related pathways. This will provide a framework for interpreting this vast amount of data. The three major mechanistic neurobiological pathways appear to be vascular, inflammatory and endocrine, each of which each has links to extra-brain systems and which interact with each other through immune-inflammatory mediators.
Mast cells are found perivascularly in all tissues including the brain, especially in the meninges, amygdala and hypothalamus. Mast cells are involved in allergies, but also in mastocytosis, as well as many inflammatory and neuropsychiatric diseases where they are stimulated by neurohormonal triggers, especially the stress-related neuropeptides corticotropin-releasing hormone (CRH) and neuropeptide Y. Histamine and inflammatory cytokines released further stimulate microglia thus causing focal brain inflammation and leading to decreased cognition, memory and ability to concentrate, commonly known as “brain fog.” This state characterizes patients with autism spectrum disorders, irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia syndrome (FMS), generalized anxiety disorder, mast cell diseases and “minimal cognitive impairment,” an early clinical presentation of Alzheimer’s disease, all of which worsen by stress. Brain Fog is increased by chemotherapeutic agents and opioids administered to cancer patients and others with severe bone pain such as in arthritis, FMS or sickle cell disease. Recent evidence supports the potential use of certain natural flavonoids for the treatment of neuropsychiatric and neurodegenerative diseases. In particular, the flavone luteolin has anti-oxidant, anti-inflammatory, microglia inhibitory properties, while also increasing memory. In particular, luteolin inhibits release of pro-inflammatory molecules from both human mast cells and microglia, thus exerting neuroprotective actions. In an open-label case series study, a liposomal luteolin formulation in olive fruit extract substantially reduced brain fog and improved functionality in patients with mastocytosis.

Acknowledgements: Patents US7,906,153; US8,268,365; US7,906,153 and US9,050,275; US9,176,146 (awarded to TCT)

References:


**L2.3 | Treatment development for neuropsychiatric symptoms in Alzheimer’s with a focus on agitation**

**C.G. Lyketsos, E. Plank Althouse**

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Neuropsychiatric symptoms (NPS) including psychosis, agitation, apathy, depression, and sleep disorders are hallmarks of Alzheimer's disease and related dementias resulting directly or indirectly from brain damage produced by the underlying disease. NPS are associated with worse outcomes for patients and caregivers, including accelerated time to severe dementia, institutionalization, and earlier death. Earlier efforts approaching these as conventional DSM ICD conditions (e.g., major depression, bipolar disorder, psychotic disorder) led to importing therapies from other areas of psychiatry. While there has been partial success with these efforts, use of antipsychotics, antidepressants, anticonvulsants, or benzodiazepines has proven too risky or ineffective. Additionally, there has been limited use of caregiver and environmental interventions (sometimes referred to as nonpharmacologic treatments). In the last decade, significant advances have occurred in understanding the pathogenesis of NPS leading to renewed promise for the development of better and safer therapies. These capitalize on parsing out heterogeneity, and applying sequential approaches combining general or specific nonpharmacologic approaches with pharmacologic approaches targeted to subpopulations of patients most likely to benefit from individual therapies. This presentation will provide an overview of the background above and focus on recent developments in treating agitation in patients with Alzheimer's disease illustrating the emerging success of this novel approach.
Symposia Presentations

SYMPOSIUM 1
Atypical clinical presentations in dementia

S1.2 | Posterior presentations (posterior cortical atrophy, corticobasal syndrome) in Alzheimer’s disease
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Alzheimer disease (AD) is the most common neurodegenerative dementing disorder. Its’ typical phenotype comprises a slowly progressive predominantly amnestic syndrome, particularly of recent events, in elderly patients (>65 years). However, clinicopathological studies have highlighted the significance of diverse clinical phenotypes of AD, most commonly in younger patients. These phenotypes are the behavioural – frontal variant, the primary progressive aphasia syndrome (most commonly of the logopenic type), as well as the posterior syndromes, namely corticobasal syndrome and posterior cortical atrophy. CBS is characterized by apraxia, alien limb phenomenon, cortical sensory deficits, dystonia, myoclonus and a predominantly akinetic – rigid extrapyramidal syndrome. The underlying disease of CBS is most commonly corticobasal deneration, although AD, FTLD-tau (frontotemporal lobar degeneration with tau pathology), PSP (progressive supranuclear palsy), FTLD-TDP (frontotemporal lobar degeneration with underlying TDP-43) may also manifest as CBS. PCA on the other hand manifests with elements of the Balint syndrome (ophthalmokinetic apraxia, optic ataxia, simultanagnosia) as well as elements of the Gerstmann syndrome. AD, DLB (dementia with Lewy bodies), CBD and rarely prion disease are the most common disorders underlying PCA. Aim of the presentation is to highlight the diverse clinical manifestations of the posterior AD syndromes and document differences in imaging (both structural and functional) and neuropsychological profiles. The importance of both imaging and CSF biomarkers in establishing the underlying pathology in patients with the aforementioned phenotypes will be discussed.

S1.3 | Alzheimer’s disease presenting as primary progressive aphasia
G. Paraskevas
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Although Alzheimer’s disease (AD) usually presents as an amnestic dementia, it may present rarely (~10%) as a progressive language disorder, i.e. primary progressive aphasia (PPA). The language disorder dominates the clinical picture for at least 2 years. During that period, other cognitive domains are not (or only minimally) affected, and the difficulty in everyday living is due to the aphasic disorder. During the last few years it has been repeatedly stated that AD is associated with the logopenic type of PPA, in contrast to the Frontotemporal Lobar Degenerations, which are associated with the non-fluent agrammatic or semantic types of PPA. Indeed, the most frequent type of PPA in AD (about 50%–60%) is the logopenic one. However, increasing evidence suggests that 25%–30% of AD PPA patients may present with the semantic type and ~10% with the non-fluent agrammatic type. Thus, although the logopenic is the most common type of PPA in AD, logopenic PPA and AD are not synonymous.
SYMPOSIUM 2
Rehabilitation and recovery of people with schizophrenia

**S2.1 | Biological interventions in individuals with schizophrenia. The recovery process. State of art**

P. Georgila\(^1,2\)

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Biological interventions are the main therapy for individuals with schizophrenia. The implementation of evidenced based biological interventions is obligated today. This factor leads to the improvement of positive, negative symptoms and to improvement of the quality of life. The above procedure increases the possibility for the participation of the individuals of schizophrenia in an evidenced based rehabilitation program or an individual cognitive behavioural therapy.

**S2.2 | Biological interventions in negative symptoms. State of art**

M. Printzou

Department of Psychiatry, “G. Gennimatas” General Hospital, Athens, Greece

Negative symptoms are divided into primary and secondary symptoms. Negative symptoms are secondary, if they are a result of side effects of medication or are a psychological reaction to psychotic symptoms or a consequence of comorbidity depression. In the absence of these factors, negative symptoms are primary and associated with the disorder. Negative symptoms are strong predictors of poorer prognosis, poorer social outcome and poorer quality of life. They are present in the prodromal phase, during psychosis and after the remission of positive symptoms. The biological interventions in negative symptoms will be discussed.

**S2.3 | The implementation of IPT in chronic inpatients with schizophrenia**

K. Poulou\(^1,2\)

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Schizophrenia is the most important and enigmatic disease which assault the human beings. It involves thought, affect and behavioral disorders and only a multifactor therapy plan would have been likely to succeed. The Integrated Psychological Therapy (IPT) is a rehabilitation program for schizophrenia patients with negative symptoms. It consists of 5 subprograms and it is focused on the improvement of cognitive impairments, social skills and problem solving.

The present pilot study has been engaged at the Asklepieion Psychiatric Hospital in Athens. Its purpose is the implementation of IPT in chronic inpatients schizophrenic people. The study is consisted of 8 subjects, 4 in the IPT group and 4 in the control group (treatment as usual – pharmacotherapy and supportive therapy). Results have indicated a positive improvement of the cognitive impairments to the chronic inpatients who have attended the IPT group (a program of 20 sessions) as well as a reduction of their negative symptoms.
S2.4 | Cognitive behavioral psychotherapy and rehabilitation in schizophrenia patients. The recovery process. State of art
S. Rakitzi1,2
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The evidenced based psychotherapeutic interventions are obligated today. The combination of them with the biological interventions lead in the long term to the improvement of the cognitive functions (neurocognitive and socialcognitive functions), of positive, negative symptoms and the general psychopathology and to the improvement of functional outcome and the quality of life. This procedure leads to a recovery process, which plays an important role for the reintegration in the society.

The evidenced based cognitive behavioral interventions as well as rehabilitation programs will be presented and discussed. The implementation of Integrated Psychological Therapy and its efficacy in the psychiatric department for adults of the General Hospital “G. Gennimatas” in Athens will be discussed.

SYMPOSIUM 3
New perspectives on trajectories of NeuroPsychiatric Symptoms (NPS) over the course of dementia and relationships with cognition and function

S3.1 | Trajectories of NPS in pre-clinical NACC (National Alzheimer Coordinating Center) participants and conversion to MCI and dementia
J.-M. Leoutsakos
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We present data from over four thousand NACC (National Alzheimer Coordinating Center) participants from 35 past and present Alzheimer Research Centers in the US. Participants were aged 60 or older, were cognitively normal at baseline, and had between one and eight annual follow up visits. Each visit included cognitive testing and the NPI-Q (Neuropsychiatric Inventory-Questionnaire).

Using data from baseline NPI-Q domains, we identified four classes neuropsychiatric symptoms: irritable, depressed, complex (depression, apathy, irritability and nighttime behaviors) and asymptomatic. Even after adjusting for cognitive test performance, we found that membership in a non-asymptomatic class was significantly associated with risk of later diagnosis of MCI (Mild Cognitive Impairment) or dementia. Hazard ratios were 1.76 (95% CI: 1.34, 2.33) for the irritable class, 1.90 (95% CI: 1.49, 2.43) for the depressed class, and 3.20 (95% CI: 2.24, 4.58) for the complex class (See Leoutsakos, et al 2015).

In further exploring those data, we found that individuals who remained in one of these higher-risk classes at a subsequent visit, or who transitioned into one of these classes, were also at greater risk for conversion. As such, we sought next to characterize course of NPI scores over time. We used growth mixture modelling to identify latent classes of total NPI score trajectories over time. We then assessed risk of conversion to MCI or dementia as a function of trajectory class membership. We also assessed baseline risk factors for trajectory membership.
We next sought to model trajectories of single NPI domains including depression and apathy. We fit growth mixture models to identify latent classes of NPI domain trajectories, and modeled risk of conversion of risk of conversion to MCI or dementia as a function of trajectory class membership. We will also demonstrate graphically the evolution and natural history of each NPI domain.

Acknowledgements: NACC is funded by the National Institute on Aging (U01 AG016976).

**S3.2 | The disconnection of cognitive and psychiatric symptom trajectories in the Clinical Course of Cognition and Comorbidity (4C) study dementia cohort**

**M.L. Haaksma, J.-M. Leoutsakos, P. Aalten, J. Bremer, M.G.M. Olde Rikkert, R.J.F. Melis**

On behalf of the 4C Study Group

**Introduction:** Dementia is a syndrome affecting multiple aspects of life through cognitive symptoms as well as diminished functional abilities and behavioral changes. Heterogeneity of symptom development causes high uncertainty for patients about their future. Despite this fact, the three previously mentioned domains are seldom studied simultaneously. In order to gain more insight in patients’ prognosis, this study investigates how trajectories over time in these different domains are interrelated within individuals, taking into account dementia severity.

**Methods:** In the Clinical Course of Cognition and Comorbidity study, 331 dementia patients were followed up yearly for a maximum of three years. Cognitive status was measured using the Mini Mental State Examination (MMSE), functional abilities were recorded according to the Disability Assessment for Dementia (DAD) and neuropsychiatric symptoms were scored using the neuropsychiatric inventory (NPI). Dementia severity was rated using the Clinical Dementia Rating (CDR) scale, and the EuroQol 5-D VAS was used to assess QoL. We investigated the relationships in the time course of the various dementia domains using time-varying covariates in random effects multilevel models.

**Results:** Baseline DAD was correlated significantly with MMSE score at baseline ($r = 0.23; p < 0.001$) and with baseline NPI score ($r = -0.36; p < 0.001$). Over time, higher MMSE scores were associated with higher DAD scores ($\beta = 1.69; p < 0.001$), but not with NPI scores ($\beta = -0.16; p = 0.129$). As expected, all three domains were associated dementia severity. In addition, decreased DAD and increased NPI were both associated with increased quality of life, while MMSE was not.

**Discussion:** Cognitive and functional abilities appeared to be highly interrelated, both cross-sectionally and longitudinally, in contrast to cognitive and psychiatric symptoms which appeared to be unrelated. While cognitive and functional trajectories tend to decline over the course of dementia, trajectories of NPS show more complex patterns of increasing and decreasing severity.

**Conclusion:** These results show that not all domains develop in the same manner over time and suggest that the heterogeneous presentation of dementia may emerge from an interplay of multiple factors. This underlines the importance of a multidimensional research perspective on dementia, focusing not only on disease characteristics, but also on personal contextual factors such as their physical, social and psychiatric health.
S3.3 | Trajectories of agitation and its predictors in AD patients from the European ICTUS cohort
P.-J. Ousset
Unité Aigue Alzheimer, Equipe Régionale Vieillissement et Prévention de la Dépendance, Gérontopôle, Pr Vellas CHU Toulouse, INSERM UMR 1027, Toulouse, France

Objective: To study associated factors that were present six months prior to the onset of an episode of agitation and aggression among community dwelling AD patients over two years of follow up.

Methods:
Study design: Data presented will be from the Impact of Cholinergic Treatment USe (ICTUS) study. The ICTUS Study is a European longitudinal observational study with 6-monthly follow-up visits over a 2-year period. Patients were recruited from February 2003 until July 2005 by 29 expert outpatient memory clinics of mostly academic hospitals in 12 European countries.
Population studied: participants had to be diagnosed with probable AD according to NINCDS-ADRDA criteria with a Mini-Mental-State-Examination (MMSE) score of 10–26. Patients were living at home at baseline and had to be cared for by an informal caregiver.
Data collection: At baseline and twice yearly, patients underwent comprehensive clinical and neuropsychological assessment, including MMSE, ADAS-cog, physical disability, and assessment of neuropsychiatric symptoms (NPS) based on the Neuro-Psychiatric Inventory (NPI). Comorbidities and medication use were also recorded, as well social status and caregiver situation.
Analyses: Sociodemographics, cognitive status, physical status, disease severity, and NPS were analyzed at baseline and then, every six months over the 2-year follow-up. In order to study factors associated to the onset of an episode of agitation, a multivariate multi-level model was used. The variable of interest was the severity of the item agitation/aggression (A/A) of the NPI. The score of this item is the result of the frequency multiplied by severity score of the A/A NPI item. This variable was coded as a continuous variable.

Results: 1375 patients were included in this cohort. Frequency of A/A NPS varied from 30% to 34% at each visit. Two factors were found to be independently associated six months prior to the onset of A/A: 1) the presence of affective/mood NPS (anxiety, depression and/or irritability) was associated with an increase in the severity of the A/A symptoms of 0.89 point [coefficient 0.89; (IC 95%): 0.48-1.30, p<0.001] and, 2) a higher caregiver burden was associated with an increase in the severity of the A/A symptoms of 1.08 points (coefficient 1.08; IC 95%: 0.69-1.47, p<0.001).

Conclusion: The results of our study highlight the importance of the effect of NPS and a high caregiver burden on the onset of A/A NPS over a 2-year follow up. The identification and the optimal treatment of affective NPS as well as the evaluation of the caregiver could be beneficial to the management of A/A symptoms in AD community-dwelling patients.

S3.4 | Agitation and quality of life in people with dementia living in care homes
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Introduction: Agitation in people with dementia is common; it is a behaviour which is generally thought to be related to inner distress and comprises verbal, vocal or motor activity for which there is no obvious
cause. It is thought to result from unexpressed, unfulfilled or unknown needs such as boredom, discomfort or pain in a person with dementia (Livingston et al 2014). It is more common in those with severe dementia. It is difficult for families to cope with agitation and it therefore often leads to care home admission. This means there are many people living with dementia and with symptoms of agitation in care homes.

A recent systematic review found that there are only few high quality studies that investigate associations of quality of life of people with dementia living in long-term care facilities. These suggest that agitation is related to lower quality of life in care homes (Beerens et al 2013).

In the Managing Agitation and Raising QUality of life in dementia (MARQUE) study, we aimed to examine our hypothesis that agitation using the Cohen Mansfield Agitation Inventory (CMAI) is inversely associated with staff rated quality of life using DEMQoL, and explore our hypotheses that it is related to more severe dementia, family and resident rated quality of life, less available activities (boredom) and more prescription of analgesics.

Methods: We recruited 97 care homes clusters in England to the MARQUE cohort study and collected data from people with dementia, their staff carers and relatives. This included demographics, dementia severity, DEMQoL agitation using the CMAI and neuropsychiatric inventory (NPI), care home activity, frequency of family visits and characteristics of the care home.

Analysis: Random effects models to account for care home clustering controlled for age, sex, dementia severity and care home type. We classed CMAI >45 as clinically significant agitation.

Results: 1489 residents, 1054 relatives and 1696 staff members consented to the study. Residents were mostly female (65%), white (95%), and with a mean age of 85 (SD 9). 38% had severe dementia, median CMAI score was 43 (IQR 39, 55); 40% had clinically significant agitation and 15% scored the minimum on the CMAI. Median staff proxy quality of life was 104 (IQR 95, 110). Agitation was significantly inversely related to quality of life assessed by staff carers (-0.53; 95% CI -0.61, -0.46) and relatives (-0.26; 95% CI -0.33, -0.18). Activities available in care homes were not related to agitation level. Results were similar when using the NPI to define agitation.

Conclusions: Agitation in people with dementia is strongly inversely related to quality of life. It is likely that having activities available is not enough, staff require training in engaging people with agitation in them. We have begun a cluster randomised trial (by care home) to trial a staff intervention comprising training followed by supervision to manage agitation, and compare this to usual care.

References:

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SYMPOSIUM 4
Sleep and psychiatric disorders in the elderly

S4.1 | Insomnia and depression in the aged
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The prevalence of insomnia symptoms increases with advancing age. While young persons with insomnia often complain of difficulty falling asleep, older patients may complain of early morning awakening. Insomnia is a risk factor for depressive disorders, and is associated with poorer quality of life. Insomnia also serves as a risk indicator for elevated risk of suicide death in the elderly. Persistent insomnia symptoms serve as an indicator of increased risk of depressive relapse in those depressed elderly who have otherwise had a good antidepressant response to psychotherapy. For these reasons, insomnia requires treatment in older depressed patients. Selective serotonin reuptake inhibitors (SSRIs) are unreliable as monotherapy for improving insomnia complaints in depressed elderly, even when SSRIs are otherwise successful in treating depression. Similarly, ECT and rTMS do not have intrinsic benefits for insomnia apart from their antidepressant effect. Hence consideration should be given to adjunct cognitive behavior therapy for insomnia for depressed elderly patients, or the judicious use of hypnotic medications.

S4.2 | Hypersomnia and mental health in the elderly
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Aging is often associated with complaints of difficulties with sleep. There are a variety of conditions that may account for the sleep difficulties experienced by many older adults, including specific sleep disorders, circadian rhythm disturbances, and medical and psychiatric comorbidities. Hypersomnia includes a group of disorders in which the primary complaint is excessive daytime sleepiness. The severity of daytime sleepiness needs to be quantified by subjective scales (e.g. Epworth sleepiness scale) and objective tests such as the multiple sleep latency test. Hypersomnia does not correspond to an individual clinical entity but includes numerous different etiologies of hypersomnia for example hypersomnia due to medical condition (neurologic or psychiatric disorder e.g. major depression), hypersomnia due to drug or substance, sleep-related disordered breathing and periodic leg movement disorders, narcolepsy with and without cataplexy, idiopathic hypersomnia with and without long sleep time, recurrent hypersomnia, behaviorally induced insufficient sleep syndrome, hypersomnia not due to a substance or known physiologic condition. Before making a diagnosis the patient should receive a complete blood count (CBC), screening biochemistry tests, and thyroid-stimulating hormone tests to exclude common physical disorders that may present with complaints of excessive tiredness, often expressed as excessive sleepiness by patients. A drug screen is indicated if substance-induced sleep disorder needs to be ruled out. If an underlying cause of hypersomnia is suggested, appropriate consultations with a neurologist, pulmonologist, and psychiatrist should be obtained.
Critics of electroconvulsive therapy (ECT) have maintained that ECT is damaging or disabling to patients who receive it. To the contrary, our prior research in the area of ECT and quality of life (QOL) and function have shown that the receipt of ECT improves reports of QOL and function in depressed patients of mixed ages. However, before now, QOL studies have not been available in samples of elderly depressive receiving ECT. We conducted a study of 240 depressed elderly patients (> 60 years old) who received high dose ultra-brief (UB) right unilateral (RUL) ECT with pre and post measurements of QOL with the Short Form 36 (SF36). We found large improvements in QOL after ECT for the overall sample, with the improvements best explained by improvement in depression symptoms, while no aspect of change in QOL was related to pre-ECT intelligence, or changes in memory or executive function. Of these 240 patients, 120 remitters were randomized to continuation therapy with lithium and venlafaxine versus ECT combined with the same medications. Patients were followed in continuation therapy for 24 weeks. At the end of 24 weeks, those assigned to ECT + medications had superior QOL outcomes as compared with those assigned to medications alone. Changes in QOL during continuation therapy were explained by changes in depression symptoms, and had minimal relationship to memory or executive functioning. We conclude that high dose, UB RUL ECT produces large and reliable improvement sin QOL in depressed elderly, and that continuation ECT with medications are superior to medication alone in maintaining a high QOL during the continuation phase of treatment.

Bipolar disorder accounts for 10% to 25% of all geriatric patients with mood disorders and 5% of all patients admitted to geropsychiatric inpatient units. Bipolar disorder in the elderly is a disabling illness frequently characterized by comorbid psychiatric disorders including substance abuse, alcohol use disorders, dysthymia, generalized anxiety disorder, panic disorder and delirium. Mania also has associated hyperactivity, aggression, violence and noncompliance with medical and physical care which can be particularly debilitating in the elderly. ECT is an effective treatment for all phases of bipolar disorder, and a review of 589 patients with acute mania found that 80% of the patients either remitted or were markedly better (Mukherjee, Sackeim et al. 1994). However, only a few studies have focused on elderly bipolar patients and these studies will be reviewed as well as studies describing the risks and benefits of concomitant medications including neuroleptics, anticonvulsants and lithium.

References:
Old-age depression

S6.1 | Epidemiology and clinical manifestations
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Depression is one of the most common disorders of the elderly. According to epidemiological studies 10-15% percent of the elderly living in the community have depressing symptoms and about 0.5-3% percent suffering from major depression. It been estimated that 10% of the elderly hospitalized with physical disorders and 17-35 % living in residential homes experiencing depression.

The clinical presentation of depression is characterized by symptoms such as depressive mood, feelings of helplessness and hopelessness, loss of interest in daily activities, anxiety, feeling agitated, restless or retard, feeling fatigued, loss of energy, sleep changes, either insomnia or oversleeping, appetite or weight changes, significant weight loss or weight gain, concentration problems, trouble focusing, making decisions, or remembering things. Unexplained aches and pains - an increase in physical complaints such as headaches, back pain, aching muscles, and stomach pain. Depression is a major risk factor for suicide.

Diagnosis of depression is based on DSM-5 and ICD-10 criteria/classification.

Persistent depression is a risk factor for dementia in the elderly. The etiology of depression in the elderly is a combination of multifactors, is by its very nature a heterogeneous disorder. Depression is a chronic, recurring, multifactorial, and life-threatening disorder, which represents a collection of psychological, neuroendocrine, physiological and behavioural symptoms. It's important to be aware that some
medications or medical problems can cause depression in older adults, either directly or as a psychological reaction to the illness.

It is now clear that there is a strong relationship between depression and vascular disease, at least in the form of cerebrovascular disease. Vascular depression and post stroke depression, as a unique subtype of late-life depression.

Clinical presentation of vascular depression are apathy, general slowing down, neglect of responsibilities and self-care, withdrawing from family and friends, decline in day-to-day ability to function, being confused, worried and agitated, inability to find pleasure in any activity, cognitive dysfunction and impairment, deficits in executive functioning are often present and must be evaluated very carefully.

Typically, elderly patients with depression do not report depressed moods but instead present with less specific symptoms such as insomnia, anorexia, and fatigue. Elderly persons sometimes dismiss less severe depression as an acceptable response to life stress or a normal part of aging. There is poor response to treatment and in general can be antidepressant treatment resistant.

Geriatric Depression is treatable. Effective management requires a biopsychosocial approach, combining pharmacotherapy and psychotherapy. Pharmacotherapy for acute episodes of depression usually is effective and free of complications. Especially in the elderly we often advice “start low, go slow” Thus, therapy for older patients should be continued for longer periods than are typically used in younger patients. Early treatment and prescribing adequate dosages appropriate for the age and other comorbidity issues is necessity.

Medication is appropriate not only for primary depression but also for depression associated with medical conditions such as cancer, heart and pulmonary diseases, arthritis, stroke, and parkinsonism. However, the physician must consider carefully how the metabolism of the drug may be affected by physiologic changes resulting from aging and other medical problems, so close follow-up and review of side effects are important when prescribing antidepressants.

Geriatric depression is not a part of aging. Therapy generally results in improved quality of life, enhanced functional capacity, and possible improvement in medical health status, increased longevity, and lower health care costs.

S6.2 | Psychotic major depression in old age: An overview
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Psychotic depression (PMD) in the elderly is highly prevalent in inpatient settings, causes great suffering and disability and also is a difficult-to-treat condition. Nevertheless, its differences from non-PMD in regard to the above-mentioned key features as well as its nosological status need further investigation. PMD in older people compared to non-PMD has been shown to present with overall more severe depressive symptoms, greater psychomotor disturbance, more guilt feelings, more depressive episodes with psychotic features, poorer prognosis, more severe executive dysfunction associated with prefrontal and fronto-temporal brain atrophy, and lower serum dopamine $\beta$-hydroxylase activity. No differences were found in regard to the efficacy of an antidepressant plus antipsychotic combination vs. antidepressant monotherapy in the acute as well as in maintenance treatment. Older patients with PMD present more somatic complaints and delusions of hypochondriacal and impending disaster content and a lower comorbidity with anxiety disorders compared to PMD in younger adults. In conclusion, PMD in older people
is characterized by higher severity in most clinically important key-features than the non-PMD. Nevertheless, available evidence is still insufficient for the conclusive elucidation of its nosological status. Finally, the differences between PMD in older and younger patients may be attributed to biological and psychosocial changes of old age.

**S6.3 | Pharmacological treatment of old age depression: The need for guidelines**

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Late-life depression (LLD) refers to depressive syndromes, as defined in the American Psychiatric Association’s Diagnostic and Statistical Manual (DSM-IV) and in the International Classification of Diseases (ICD-10), that arise in adults older than 65 years old. Studies of community-residing older adults show a decline in the overall prevalence of depression compared to middle-aged adults. However, medically ill, disabled older adults have a high prevalence of depression [1]. In particular, 15% of elderly population, 10-12% of medical inpatients and 12-14% of nursing home residents have major depression (MD) and larger numbers experience less severe depressive syndromes [1,2].

Late-life depression is associated with significant functional decline, family stress, greater risk of medical illness, reduced recovery from illness, and premature death from suicide or other causes [3]. It is important that clinicians realize that depression in the elderly is treatable and that treatment can result in major functional, social, and health gains.

In the literature, two systematic guidelines for the pharmacological treatment of LLD have been published until now. One in 2001 (Pharmacotherapy of depression in older patients: a summary of the expert consensus guidelines. Alexopoulos GS, et al. 2001) [4] and one in 2006 (National guidelines for seniors’ mental health. The assessment and Treatment of Depression. Canadian coalition for seniors’ mental health. 2006) [5]. Since that time, additional studies have been conducted and new treatments have been available. Recent reviews of the literature have confirmed the efficacy of antidepressants for LLD [6], highlighting their protective effect against suicide in those aged 65 years or older [7]. Although the main points of the previous recommendations are still valid, an update with recent treatment developments is needed.

**References:**

1. Alexopoulos GS, Kelly RE. Research advances in geriatric depression. World Psychiatry 2009; 8:140-149
2. Λύκουρας Λ, Πολίτης Α, Γουρνέλλης Ρ, Μαΐλης Α. Στοιχεία Ψυχογηριατρικής. Βήτα Ιατρικές Εκδόσεις ΜΕΠΕ, Αθήνα 2011
Suicide prevention in hospitalized middle aged and older adults

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Suicide rates in middle-aged and older adults are alarmingly high. Patients hospitalized following acute suicidal ideation or attempt are at high suicide risk during the early post-discharge period, especially within the first 3-months after discharge.

Suicidal ideation and behavior may be conceptualized as failed attempts to regulate emotions. Therefore, by improving cognitive reappraisal, a well-documented and effective emotion regulation strategy, we expect to reduce suicide risk. We will present the development and pilot testing of an emotion-regulation intervention for middle-aged and older adults discharged after a suicide-related hospitalization. The intervention identifies triggers of negative emotions that are associated with suicidal ideation and suicide attempt and develops simplified, easy to use cognitive reappraisal techniques to reduce these negative emotions. The intervention employs environmental adaptations/aids to assist patients in utilizing cognitive reappraisal techniques between sessions (WellPATH personalized tablet app, written step-by-step plan, phone calls).

SYMPOSIUM 7
What’s new in older age bipolar disorder? Clinical assessment, treatment, and the brain

S7.1 | Clinical assessment and evidence based treatments for OABD

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Despite an expected increase in the world’s aging bipolar population, the assessment, clinical course and treatments for individuals with older age bipolar disorder (OABD) have been vastly understudied. This presentation will discuss the epidemiology of older adult bipolar disorder, describe a practical clinical assessment approach and review evidenced based treatments for geriatric mania, depression and maintenance.

Although the prevalence of OABD in the U.S. population greater than age 50 is approximately 0.5-1%, rates increase in specific clinical settings. For example, OABD represents approximately 6% of all geriatric psychiatry outpatient visits, 8-10% of hospital geriatric psychiatry inpatient admissions, 3% of nursing home residents and 17% of older adults with psychiatric symptoms presenting to the emergency room [1,2,3].

Age of onset of bipolar disorder has significant clinical implications. For example, individuals with late-onset bipolar illness are more likely to be women, less likely to have a family history of bipolar disorder, and more likely to have cerebrovascular risk factors or disease. The symptoms of bipolar disorder do not typically attenuate over time. Individuals with OABD are at increased risk for functional decline and overall morbidity and mortality.

The clinical assessment of the older adult with bipolar disorder requires consideration of aging-related factors such as major neurocognitive disorder, medical and psychiatric co-morbidity, medications and the psychological sequelae of cumulative medical burden, cognitive decline and functional impairment. The
clinical interview and history, including collateral information gathered from family members and health care providers, are essential to the evaluation of OABD. Cognitive impairment is a core feature of bipolar disorder, occurring in approximately 40-50% of euthymic, OABD, and associated with disability and poor outcome. Cognitive impairment has been identified in the domains of attention, cognitive flexibility, information process speed, memory and semantic and verbal fluency. Vascular burden and hospitalizations are risk factors for cognitive dysfunction in OABD.

Research on pharmacotherapy in OABD is limited as older adults are often excluded from randomized controlled registration trials (RCTs) due to the increasing risk of medical complications with advancing age. Nevertheless, post-hoc analyses of older adult cohorts from such trials support the use of similar first line treatments recommended for younger adults with bipolar disorder. Age associated decreases in drug absorption, body distribution, metabolism and excretion complicated by polypharmacy will affect the pharmacokinetics and pharmacodynamics of medications impacting the central nervous system.

Few psychosocial interventions or specific psychotherapies for OABD have been studied systematically. Current practice is focused on psychoeducational techniques and cognitive behavioral psychotherapy during episodes of bipolar depression and to prevent recurrent mood relapse. Such psychotherapeutic techniques are informed primarily by extrapolation from mixed age studies. "The Helping Older People Experience Success" (HOPES) intervention was compared in a two year randomized trial with treatment as usual (TAU) and found to improve social skills, community functioning, self-efficacy, leisure and recreation in older adults with severe mental illness, including bipolar disorder[4].

References:

S7.2 | Insights into cognitive impairment in Older Age Bipolar Disorder (OABD) through phosphorus spectroscopy (31P MRS) of the brain

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Patients with older age bipolar disorder (OABD) have well documented cognitive deficits, particularly in the domain of cognitive control. However, cognitive control is composed of discrete sub-domains, and performance in these sub-domains may be mediated through different neural substrates. We examined the relationship between levels of phosphorus metabolites measured by 31P 3D MRSI in the brain and two distinct tests of cognitive control; Stroop Interference (a test of response inhibition) and Trail Making Test B (a test of set shifting or multitasking) in both OABD and age-matched normal controls.

We studied 5 OABD patients (4F: 1M; mean age ± SD = 61.40 ± 4.39 years) and 6 normal elderly patients (4F: 2M; mean age ± SD = 60.17 ± 3.25 years). Subjects completed the cognitive tasks and raw scores were converted to age, sex and education adjusted t-scores. High contrast, T1 weighted sagittal and axial images sets of the entire brain, and 31P, 3D MRSI data in a 3x4x7 voxel submatrix were acquired at 4 Tesla using a dual-tuned, proton phosphorus TEM head coil. Our hypotheses concerned 7 (beta-NTP, PCr, Pi, PCho, PEtN, GPCho and GPEtn) of the 11 phosphorus-containing molecules that were quantified by our spectral fitting algorithm. Linear, mixed-effects models with random intercepts for subjects were
constructed for individual neuropsychological tests (Stroop Interference and Trails B) for each of the 7 phosphorus metabolites assessed. Fixed effects included diagnosis, neuropsychological test t-score, partial volume, tissue type, and total phosphorus signal. We tested first for three-way interactions between neuropsychological score, condition and tissue type (assessing for evidence of difference in tissue-specific associations between LLD and controls), and if these were non-significant, tested the significance of the interaction of neuropsychological score and tissue type (assessing for evidence of tissue-specific associations across LLD and controls). Significant interactions overall served as gatekeepers for individual tissue and diagnostic specific tests.

Gray matter beta-NTP (a surrogate of ATP) levels were 19% lower in OABD compared to age-matched controls (t(44) = 2.28; p = 0.021). We found a tissue specific, positive relationship between PEtn and better performance on the Stroop Interference test in OABD that we did not observe in the age-matched control group (t(177) = 2.56; p = 0.011). We also observed a tissue specific, positive relationship between PEtn and better performance on the Trails B task in our control population (t(108) = 2.07; p = 0.041). We did not observe any relationships between our measures of cognitive control and any of our bioenergetic metabolites (beta-NTP, PCr or Pi).

Reductions in gray matter beta-NTP suggest impaired mitochondrial function in OABD. Measures of two different aspects of cognitive control (Trails B and Stroop Interference) showed different dependencies on the state of phosphoethanolamine (a cell membrane precursor) in the brain.

S7.3 | Accelerated brain aging in bipolar disorder? Using multi-modal neuroimaging to assess age-related changes

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Bipolar disorder (BD) has been characterized as neuroprogressive. Several cross-sectional studies and one longitudinal study have suggested a steeper slope of age-related change in individual brain indices among those with the disorder compared to those without. However, aging of the brain is likely to be multi-dimensional, with different rates and shapes of trajectories depending on the region or the measure (e.g., structural versus functional). One recent study found that “brain age” based on a multivariate model of structural measures was significantly older than chronological age in BD. We aimed to extend this work by examining brain age based on multiple imaging modalities as well as clinical correlates. Magnetic resonance images of brain structure and function were collected from 46 euthymic individuals with BD and 80 healthy comparisons (HC; age range = 30-80 yrs), including measures of regional cortical surface area and thickness, regional subcortical volume, white matter tract integrity, white matter hyperintensities, regional cerebral blood flow, and regional task-based and task-free blood oxygen level dependent signal. Multi-modal measures were combined to create a predictive model of chronological age in the HC group in order to calculate a “brain age” for all participants. Cross-validation was used to yield stable predictions. Chronological age was subtracted from brain age to create an age discrepancy score. Within a matched subsample (HC n=53; BD n=46), we compared group discrepancy scores and calculated correlations with clinical variables. With a linear model, age of the HC group was estimated within +/- 8.8 years; the most predictive measures were regional brain size, cerebral blood flow and white matter hyperintensities, and, less commonly, white matter tract integrity, regional functional response, or functional connectivity. BD brain age was older than chronological age by about 7 years, significantly different from HC (p=0.02). Among BD, those with more lifetime manic episodes had older brain age compared to their actual age,
after accounting for actual age (p = 0.02). There was no relationship with gender, symptom severity, duration of illness, lifetime depressive episodes, illegal drug use, or lithium use. Ongoing analyses will examine performance of other predictive models and determine which brain features contribute most to group differences. The findings will be discussed in terms of implications for the theory of neuroprogression in BD.

**S7.4 | Could lithium prevent the bipolar disorder brain age-related decline?**


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Bipolar disorder (BD) is associated with an increased rate of dementia and age-related decline. Lithium (Li), the prototypical mood-stabilizing medication, is hypothesized to exert neuroprotective and/or neurotrophic effects that could counteract pathological processes in the brain of patients with BD. Animal studies, cross-sectional as well as longitudinal structural magnetic resonance imaging (sMRI) studies highlight evidence for positive association between Li and brain total grey matter (GM) volume but also regional grey volumes (hippocampus, amygdala, anterior cingulate, and prefrontal cortex). Li effects upon WM volumes are less explored, a few studies having identified an association between Li medication and WM integrity using diffusion tensor imaging (DTI).

We designed a multicenter, cross-sectional, brain sMRI and DTI study, in a large international sample of 272 patients with BD and 317 HC. Our objective was to test for Li influence on GM, WM and subcortical volumes. Hippocampus segmentation, and brain tissue volumes estimations (including separate estimates of total and peripheral GM, WM, and ventricular cerebro-spinal fluid volumes) were respectively completed with FIRST and SIENAX, part of FSL. Our preliminary results suggest lower total GM and WM volumes in bipolar patients compared to HC. When comparing Li versus non-Li-treated bipolar patients, a positive effect of Li on total GM and WM volumes was detected, supporting hypothesis of neuroprotective and/or neurotrophic effects of Li. Future planned analysis include the study of correlation between Li treatment duration and brain volumes; WM volumes with DTI data. We also plan to model the ageing effect on brain volumes in HC and bipolar patients separately then test Li influence on these relationships.

**SYMPOSIUM 8**

**The role of cytokines, proinflammatory mediators on the availability of precursor’s aminoacids and the tryptophan / kynurenine pathway in the pathogenesis of major neuropsychiatric disorders**

**S8.1 | Inflammation biomarkers, growth factors and kynurenine metabolites aid in stratifying patients with major depressive disorder**

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**Background:** Depressive disorders are highly heterogeneous disorders. This heterogeneity contributes greatly to diagnostic inaccuracies, a very low percentage of remitters after the initial antidepressant drug
trial, and poor predictability of suicidality, treatment response and requirement for prolonged maintenance treatment. Substantial evidence indicates that neuroinflammation contributes significantly to the etiopathology of major depression. While physiological concentrations of pro-inflammatory cytokines play an active role in maintaining synaptic plasticity, their sustained increase in untreated or inadequately treated depression is linked to impairment of synaptic plasticity and possible neurodegeneration. Experimental evidence suggests that neuroinflammation exerts a negative impact upon neurotrophin production and release thereby contributing to inhibition of antidepressant drug action. Disturbances of tryptophan (TRY) metabolism, i.e., the shunt of TRY from serotonin (5-HT) synthesis to kynurenine (KYN) formation, is considered a major etiological factor of depression. Rate-limiting enzymes of kynurenine formation, tryptophan 2,3-dioxygenase (TDO) and indoleamine 2,3-dioxygenase (IDO) are activated by stress hormones (TDO) and/or by proinflammatory cytokines (IDO) and the simultaneous presence of high producers alleles of proinflammatory cytokines genes (e.g., interferon-gamma and tumor necrosis factor-alpha).

Methods: Males and females (20-65 years of age) meeting DSM-IV criteria for primary major depressive disorder (MDD) who were physically healthy were considered. Thirty patients met inclusion criteria and were enrolled. After baseline assessments they were started on escitalopram on an open label basis. Healthy control subjects were enrolled throughout the period the MDD subjects were recruited. Rating scales were used to assess depression, state and trait anxiety, state and trait anger, stress perception, quality of life. Inflammation biomarkers and growth factors were measured by “Evidence InvestigatorTM” (Randox Technologies). Pentraxin-3 and hsCRP were measured by ELISA. Tryptophan and kynurenines were measured by HPLC. Quinolinic acid (QUIN) was analyzed using GCMS. SPSS version 20 was used for the analyses. Distributions for all biomarkers were analyzed for normality, skewedness, kurtosis, and homoscedasticity of the residuals prior to analysis. Biomarkers found to have skewed distributions were analyzed through non-parametric methods. Cluster analyses were conducted by Dr. Henk Meijerink.

Results: We observed correlations between specific symptoms of MDD and some of the biomarkers studied. Depressed mood correlated significantly with IFNγ while weight loss correlated significantly with TNFα levels. QUIN correlated significantly with guilt and QUIN/3HK correlated significantly with guilt and psychomotor agitation. Pentaxin-3 correlated with anxiety. VEGF and hsCRP predicted treatment outcome.

Two key clusters have emerged as predictive of healthy vs depressed status: The cluster showing moderate values for the neuroprotective ratio, 5HIAA, KYNA and QUIN, and a high serotonin value is highly represented in the healthy control group which could suggest that balanced values amongst the TRY metabolites represent the body’s healthy control mechanism of metabolite production. By contrast, the cluster with the highest QUIN/KYNA ratio, lowest KYNA is mostly represented in the MD group as expected. It also possesses the lowest 3HK and 5-HIAA values.

Conclusions: This is the first report that in MDD patients correlations are observed between specific depressive symptom scores and inflammation, growth factors and kynurenine metabolites. Cluster analyses can be useful in determining healthy vs depressed status and allowing further stratification of MDD patients. These results once confirmed in a larger cohort can improve diagnostic accuracy and allow prediction of treatment outcome.
**S8.2 | Proinflammatory cytokines (IL-1β, IFN-γ, IL-6, TNF-α) and oxidative stress decrease the transport of dopamine precursor tyrosine**

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**Background:** Disturbed transport of dopamine precursor amino acid, tyrosine is demonstrated in fibroblasts obtained from patients with schizophrenia and bipolar disorder. These neuropsychiatric disorders are indicated with disturbed dopaminergic, noradrenergic and serotonergic neurotransmission. The disturbed tyrosine transport could be one of the possible explanations for altered neurotransmission in these disorders. The reason for disturbed tyrosine transport in neuropsychiatric disorders is not completely understood. Over the last two decades, research and clinical studies have implicated the role of elevated proinflammatory responses and oxidative stress in the pathogenesis of many neuropsychiatric disorders. The aims of the present study were to assess the role of proinflammatory cytokines, oxidative stress on tyrosine transportation by using the human skin derived fibroblasts as model cells. In addition, this study also examines the effects of pro-inflammatory cytokines on radical oxygen species (ROS) production in human fibroblasts.

**Methods:** Fibroblasts obtained from a healthy control were used in this study. Fibroblasts were treated with proinflammatory cytokines (IL-1β, IL-6, IFN-γ and TNF-α) or oxidative stress to analyze the uptake of ¹⁴C-Tyrosine by using the cluster tray method. ROS was measured as fluorescent response after treatment with 2', 7'-dichlorodihydrofluorescein diacetate (H2DCFDA).

**Results:** The results of the present study indicate that proinflammatory cytokines, oxidative stress can decrease the transport of tyrosine. Moreover, the results of this study indicate that proinflammatory cytokines stimulate the ROS production and is shown to be associated with the decreased amino acid transportation.

**Conclusions:** This study is the first to demonstrate that Proinflammatory cytokines and oxidative stress and the interplay between them decrease the transport of tyrosine. Decrease in tyrosine transport due to proinflammatory cytokines and oxidative stress could be one of the pathophysiological factors involved in the development or progression of neuropsychiatric disorders associated with disturbed dopaminergic neurotransmission.

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**S8.3 | Influences of pro-inflammatory cytokines on precursor aminoacids transport can cause cognitive dysfunction in schizophrenia, ADHD, autism, and related CNS diseases**

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**Background:** In many studies, has been demonstrated that amino acids tyrosine and tryptophan are strongly involved in schizophrenia, bipolar disorders, autism and ADHD. In addition a large number of findings indicate that inflammation plays a crucial role in the pathogenesis of psychiatric disorders, and that cytokines are activated by psychiatric disorder, e.g. in schizophrenia and bipolar disorder is mainly activated the interleukin (IL-1β) and (IL-6) in depression. The primary aim of this presentation is to outline
and discuss findings/evidence from *in vitro* investigations, concerning the influence of pro-inflammatory cytokines/mediators, on tyrosine and tryptophan uptake.

**Methods:** For the characterization of the effects of proinflammatory cytokines on the precursor amino acids functionality, were used fibroblasts from healthy controls, treated and untreated with mixtures of proinflammatory cytokines.

**Results:** The outlines of the findings presented in this study provide evidence that the pro-inflammatory cytokines affect the functionality of neurotransmitter precursor amino acid transporters (the uptake of tyrosine and tryptophan significantly inhibits up 40%), which consequently may cause a restricted access or a mismatch of the important precursor amino acids in the brain, and cause disturbances in the central signaling systems. The dopamine and serotonin are powerful regulators at various aspects of the cognitive functions and changes in the dopaminergic and serotonergic ban systems can lead to deterioration of, among other the cognition and behavior in patients with schizophrenia, bipolar disorders, ADHD, autism, and related CNS disease.

**Conclusions:** Thus, the information’s of this presentation/symposium are very important, among other, can be useful for diagnostic and treatment purposes of neuropsychiatric disorders.

**S8.4 | Butyrate capacity for recovering of oxidative stress in the functionality of neurotransmitter precursor aminoacid transporters as well as membrane-receptor and major-carrier proteins**

I. Rangel\(^1\), R. Vumma\(^2\), N. Venizelos\(^1,3\), R. Brummer\(^1\)

\(^1\)Nutrition Gut Brain Interactions Research Centre, Örebro University, Örebro, Sweden; \(^2\)Department of Chemistry and Biomedical Sciences, Linnaeus University, Kalmar, Sweden; \(^3\)Neuropsychiatric Research Laboratory, Department of Clinical Medicine, Örebro University, Örebro, Sweden

**Background:** Our gastrointestinal tract is colonised by a large number of microorganisms, so called the gut microbiota. Alterations in the microbiota have been associated not only with gastrointestinal diseases but even neurodevelopmental disorders such as autism spectrum disorders (ASD). Furthermore, a link between behavioural modifications such as anxiety and stress-like symptoms and a disturbed gut microbiota has also been suggested. These observations substantiate the interaction that is maintained between the gut and the brain in a system nowadays called the gut-brain axis. One way of communication in this axis is based on the release of compounds from the microbiota that affect firstly the gut functioning but eventually the interaction with the nervous system. Some metabolites that are produced by bacterial fermentation in the intestine are short chain fatty acids (SCFA), namely acetate, propionate and butyrate. The latter is a primary source of energy for colonocytes but has also been involved in anti-inflammatory and anti-oxidative processes.

**Methods:** We have been assessing the effect of butyrate on the functioning of the tryptophan transport system, a biomarker for neuropsychiatric disorders. This has been done using human skin derived fibroblasts obtained from healthy individuals. Our goal is to determine to which extent an exposure to a gradient set of concentrations of butyrate, mimicking expected in *in vivo* concentrations, will counteract the disturbed tryptophan transport system resulting from an oxidative stress.

**Results:** Our first results indicate that this is the case although it seems to be the outcome of a dose-dependent effect. We also have looked at the response of receptors and membrane proteins responsible for the transport of SCFAs in human intestinal Caco2 cells.
Future experiments will include cells from ADHD and ASD patients to confirm our observations with the tryptophan-transport system.

**SYMPOSIUM 9 (ICGP PRESIDENTIAL SYMPOSIUM)**

**Current developments on depression in MCI and in Alzheimer’s disease**

**S9.1 | An introduction to behavioral and psychiatric symptoms in dementia, focusing on apathy and depression**

**A. Moríñigo**
Department of Psychiatry, University of Seville School of Medicine, Seville, Spain; ICGP President

Among the Neuropsychiatric Symptoms described in Dementia (NPS) Apathy and Depression have deserved a special attention for their high prevalence and negative impact. Current knowledge includes neuroimaging research and studies focusing on neurobiological and neurochemical bases of apathy. A focus on brain-behavior relationships, interrelationships between NPS, and evaluating the neurobiologic basis of the distinct components using multimodal imaging techniques was recommended.

Depression in AD is underscored by the observations of the high prevalence of depression in mild cognitive impairment (MCI) and AD; the prognostic significance of depression in normal aging and MCI with respect to cognitive and functional decline is an important area of research, leading to consider Depression and Dementia as a continuum.

**S9.2 | Depression in Alzheimer’s disease**

**A.M. Politis**
1st Department of Psychiatry, Geriatric Psychiatry Unit, Eginition Hospital, University of Athens School of Medicine, Athens, Greece

Depression is one of the most common BPSD. Its prevalence, in most studies is estimated to be 30%-50% among AD patients in different clinical settings. The definition of depression in AD (dAD) has been the focus of debate, which reflects the dilemma whether the diagnostic criteria for major depression from the Diagnostic and Statistical Manual of Mental Disorders (DSM) should be used or should they be adapted to better reflect the symptomatology in AD. Thus, the “Provisional Diagnostic Criteria for Depression of Alzheimer Disease” have been proposed. Depression in AD has serious and disabling effects not only on patients but on caregivers, as well, and it is associated with major adverse events on daily function and quality of life, more rapid decline and cognitive deterioration, higher mortality and reduced time to institutionalization. The serious impact of depression in AD underscores the need for more effective treatment. The medications approved for the treatment of major depression in younger individuals are the primary medications used to treat depression in AD. These treatments are based on the “monoamine hypothesis” of depression with moderate effects of approved antidepressants, as well as an increasing body of research evidence, suggest a more complex pathophysiological mechanism. The aim of the presentation is a systematic review of different treatments for Dad.
S9.3 | PATH: A non-pharmacological approach on depression in patients with MCI
D. Kiosses
Weill Cornell Medicine, Weill Cornell Institute of Geriatric Psychiatry, White Plains NY, USA

Problem Adaptation Therapy for MCI patients (PATH-MCI) is a novel psychosocial intervention designed to reduce depression and disability in older adults with amnestic MCI and depression. PATH-MCI aims to reduce depression by improving emotion regulation. To achieve its goals of emotion regulation, PATH-MCI utilizes a simplified problem solving approach; employs environmental adaptations to bypass cognitive and functional limitations; utilizes individualized emotion regulation techniques, such as the WellPATH tablet app, customized CDs, or step-by-step written plan; and incorporates monthly booster sessions. The presentation will describe PATH-MCI and present the design of a collaborative study between Cornell and Johns Hopkins University of PATH-MCI vs. Supportive Therapy in patients with amnestic MCI patients and depression.

SYMPOSIUM 10
Physiological aberrations in dementia

S10.1 | Genes and the risk for Alzheimer’s disease
D. Avramopoulos
Johns Hopkins School of Medicine, Baltimore MD, USA

Alzheimer’s disease (AD) has a significant genetic component, with first degree relatives of AD patients having 3.5 to 7.5 fold higher risk depending on the number of affected relatives. Twin studies estimate that the majority of phenotypic variance, between 60% and 80%, is attributable to genetic variation. The genetics of Alzheimer’s disease are particularly interesting as they involve genetic models that span from autosomal dominant inheritance with genetic and locus heterogeneity to complex genetics. The autosomal dominant forms involve three genes and hundreds of different pathogenic mutations including gene duplications. Gene duplications have also been described as brain specific somatic events adding another level of complexity. The complex forms of AD include variants of remarkably high effect size, the APOE alleles, and variants of small effect, which are more familiar for complex diseases. Finally there is a strong link between AD and trisomy 21, where a large proportion of trisomic patients suffer from early onset dementia likely attributable to the triplication of the APP gene on chromosome 21.

Most of the autosomal dominant forms of AD have been linked to three genes, APP, PSEN1 and PSEN2, each discovered using a different genetic approach. These have been instrumental in the development of the amyloid hypothesis. The association with APOE, discovered at around the same time, was a first link between AD and lipid metabolism, a link that has been supported by more recent genome wide association studies (GWAS) results.

GWAS have recently made significant contribution to our knowledge of Alzheimer’s genetics. Twenty-one loci explaining as much as 30% of the disease heritability have been identified, although more than 2/3 of this heritability is explained by the APOE variants alone. Most of these new associations are likely to contribute risk due to regulatory variation, which we have shown through our work on the CLU locus. New emerging tools such CRISPR/Cas9 genome editing and induced Pluripotent Stem (iPS) cells will greatly
accelerate the path from statistical associations to disease mechanisms. GWAS have also led to the
development of new analytical methods for understanding the genetics of AD such as polygenic scores.
These allow the calculation of a genetic risk for every individual, based on a reference GWAS data set.
These scores can be used to assess shared genetic liability between disorders, the relationship between
genetic liability and co-morbidities or even pathway specific contributions to the phenotype.

We are currently in the middle of unprecedented progress in the genetics of complex disorders including
AD. This progress coupled with new tools recently made available for the manipulation of genomes and
the study of human cells will unlock the translational potential of the new discoveries promising rapid
progress in the fight against AD.

S10.2 | The stress response as a predictor for Alzheimer’s disease
C.A. Munro
Johns Hopkins School of Medicine, Baltimore MD, USA

The potential contribution of stress to the development of Alzheimer’s disease (AD) has been implicated in
numerous studies. Preclinical studies show that stress causes cognitive impairment and increased levels
of AD pathology such as beta amyloid in hippocampus. In patients with AD, levels of the stress hormone
cortisol are positively correlated with the degree of cognitive impairment. Furthermore, the stress-inducing
effects on the development of cognitive impairment and AD appear to require a particular vulnerability to
stress, such as the tendency toward greater a subjective and/or physiological response to stressful
experiences. For example, in rodents, only “stress sensitive” animals develop AD pathology in response to
stress, whereas those who are “stress resistant” do not. In human studies, individuals prone to distress
(high in neuroticism) are more likely to develop AD than those who are not. Moreover, in studies
examining the effects of stress on cognition, the degree of cortisol response, rather than the experience of
stress, predicts the cognitive effects of stress.

Sex differences in both the subjective and physiological responses to stress would suggest that advancing
age places women at a disadvantage. This is of particular importance given women’s increased risk of
developing AD. Not only is the effect of age on the cortisol response to stress almost three times higher in
women than in men, stress causes memory impairment in older women but not in older men. In addition to
cortisol, the association between stress and brain-derived neurotrophic factor (BDNF) may also confer a
greater risk to females than to males. Rodent and non-human primate studies have shown that stress
reduces hippocampal BDNF in females but not males. In humans, a genetic polymorphism that reduces
BDNF transport is associated with an increased cortisol response to stress and an increased risk of AD in
women but not in men.

Taken together, these findings underscore the potential importance of considering the stress response in
explaining why women are at increased risk for AD compared to men. In this context, we examined
whether the association between stressful life events and cognitive change over approximately 11 years
differed between 332 men and 572 women (age range 30 to 99 years) in the Baltimore Epidemiological
Catchment Area (ECA) study. At ECA Wave 3 (1993-1996), participants reported distal (i.e., since 1981)
and proximal (i.e., since 1992) stressful events and underwent cognitive tests at Waves 3 and 4 (2004-
2005). In multivariable models adjusted for age, years of education, and Wave 3 cognitive test
performance, a greater number of proximal stressful life events was associated with greater decline in
delayed word recall (B=0.340; 95% CI 0.622, 0.058, p=0.018) and word recognition (B=0.383; 95% CI
0.714, 0.052, p=0.023) among women but not men. These results extend earlier findings by suggesting
differential cognitive vulnerability of women and men to stressful events. Future studies aimed at
examining sex differences in the association between stress and AD will be valuable to increase our understanding of stress as a potential mechanism underlying the development of this disease.

**S10.3 | Apathy as a personality change in dementia**

A.M. Politis  
1st Department of Psychiatry, Geriatric Psychiatry Unit, Eginition Hospital, University of Athens School of Medicine, Athens, Greece

Apathy is a disorder of executive cognition and is defined as a disorder of motivation that persists over time and should meet specific requirements. It is also encountered in several neuropsychiatric disorders; it is present in up to 90% of patients with fronto-temporal dementia, dementia with Lewy bodies and progressive supranuclear palsy, 40% of those with cortico-basal degeneration, and 20% of those with Parkinson’s disease, as well as in schizophrenia with predominant negative symptoms. In AD apathy has been associated with reduced daily functioning, caregiver distress, poor outcome and frequently complicates the course and management of dementia by contributing to functional disability and self-neglect. The results of a recent study suggested that apathy is an early sign of cognitive decline and that delineating phenotypes in which apathy and a mild cognitive syndrome co-occur may facilitate earlier identification of individuals at risk for dementia. Furthermore, it seems that patients with apathy and mild cognitive impairment progresses to dementia and it is also possible that apathy might precede mild cognitive impairment. The aim of the presentation through a phenomenological approach and a review of the neuroimaging correlates is to recognize apathy as the most characteristic personality change in neurocognitive disorders.

**S10.4 | Sleep disturbances and dementia**

D. Dikeos  
Sleep Study Unit, Eginition Hospital, University of Athens School of Medicine, Athens, Greece

Sleep, its architecture, its microstructure and its features in the elderly are impaired compared to that of young adults; this impairment is even more pronounced in dementia. In this presentation, sleep, its alterations, and sleep disorders not only in dementia but also in pre-dementia stages (i.e., mild cognitive impairment) are reviewed. In the context of neurodegeneration, sleep-wake promoting neurons may be affected, while in many of the neurodegenerative disorders, central respiratory drive and autonomic neurons are also degenerated, causing primary sleep disorders. Conversely, various recent studies suggest that common sleep disorders (i.e., insomnia, daytime sleepiness and generally decreased amplitude and robustness of sleep-wake cycle), which are mostly prevalent among the cognitively impaired people, may precede clinical symptoms of dementia and are considered as risk factors for cognitive decline and dementia. The complex interactions between sleep and dementia and the causality dilemma between the two are addressed by reviewing also the existing management strategies and the evidence of the impact of therapeutic measures of sleep disorders on dementia.
Good psychogeriatric practices in Greece

S11.2 | An integrated model for psychogeriatric care in remote areas

R. Soldatos
1st Department of Psychiatry, University of Athens School of Medicine, Athens, Greece

Telepsychiatry is a branch of telemedicine, which is defined as the intervention of a telecommunication device in the diagnosis and the overall care of patients that are separated from providers by a distance (Kuo et al 2011). Telemedicine has been utilised in order to diagnose, refer, monitor patients, exchange information and provide medical care to individuals with limited access to medical services (Hill et al 2010). It is achieved through the means of voice, video, robotic, and remote-access technology (American Telemedicine Association. “Telemedicine Defined.”).

Telepsychiatry was first used in 1959 at the Nebraska Psychiatric Institute (Hyler et al 2002). Due to recent technological advancements which facilitate the use of telepsychiatry, various studies have looked into patient and provider satisfaction (Hilty et al 2004), effectiveness (Richardson et al 2009) in adults (Hilty et al 2003), as well as specific patient populations such as children (Myers et al 2010) and geriatric patients (Rabinowitz et al 2010). These studies have produced evidence which demonstrate telepsychiatry to be in part in-person care in terms of effectiveness in diagnosis and assessment, while at the same time promoting patient access to care.

Regarding the cost analysis of telepsychiatry, various methods have been suggested. Alessi et al. 1999 suggested two types of cost analysis, an event-based technique and a cost effectiveness technique. Cost effectiveness analysis has showed mixed results (McGinty et al 2006). This is likely due to the complex nature of taking into account both direct and indirect costs involved, such as equipment, line rental costs, salaries and administrative costs, data transmission, equipment maintenance, and waiting times. Researchers have found a 70% reduction in cost (Spaulding et al 2010), while others have found a 40% reduction in cost (Doolittle et al 2011).

Several models of care have been identified in clinical practice where telepsychiatry is currently used. Such models are telepsychiatric consultations, telephone and email consultations from physician to provider of care, an integrated model of screening and telepsychiatric consultation, cultural consultation, disaster response, emergency room telepsychiatry, asynchronous telepsychiatry, mobile technology methods such as in medical homes and patients’ homes and the collaborative care model (World Health Organization 2011; Spyglass Consulting Group 2012; Richardson et al 2009).

In our presentation we are going to focus on our current model of telepsychiatric practice, which is being used to provide psychiatric care in rural areas in Greece. We are also going to discuss the facilitating as well as the impeding factors involved in the care of our patients. Finally we will be presenting our proposal for the integration of psychiatric care of old age patients in rural Greece. Our proposal is based on clinical experience accumulated through the provision of tertiary care through telepsychiatry in the past 5 years.

References:
According to Alzheimer’s Disease International Report 2015, 46.8 million people worldwide are estimated to suffer from dementia. This number will almost double every 20 years, to 74.7 million in 2030 and 131.5 million in 2050.

In Greece more than 200,000 people are living with dementia and over 400,000 caregivers are looking after them. As these numbers will increase dramatically in the years to come, dementia becomes one of the most crucial medical, societal and economic challenges in Greece.

Although there was no National Dementia Strategy in place, in accordance with European and global priorities, Greece started to organise and implement dementia programmes since 2006 but so far the resources have been limited. There are currently very few specialized community services for people with dementia: 13 Day Care Centres and three respite care facilities in Athens, Thessaloniki and smaller towns, operated mainly by the Greek Alzheimer Associations with government funding. Compared to the existing needs, services provided are woefully inadequate. There are large areas of the country, especially rural and island areas which are not covered by any specialist services or facilities. Overall, the major problem is the lack of long stay institutions and end of life centres throughout the country.

Despite their limited resources, the Greek Alzheimer Associations are very active in organising awareness campaigns, seminars for health professionals, screening programs for the public, educational programmes for carers and scientific research. Community dementia services offered by Alzheimer Associations

S11.4 | Community dementia services in Greece
P. Sakka
National Observatory for Dementia and Alzheimer’s Disease, Athens Association of Alzheimer’s Disease and Related Disorders, Athens, Greece

According to Alzheimer’s Disease International Report 2015, 46.8 million people worldwide are estimated to suffer from dementia. This number will almost double every 20 years, to 74.7 million in 2030 and 131.5 million in 2050.

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Despite their limited resources, the Greek Alzheimer Associations are very active in organising awareness campaigns, seminars for health professionals, screening programs for the public, educational programmes for carers and scientific research. Community dementia services offered by Alzheimer Associations
include: memory clinics, non pharmacological interventions for people with dementia, education and support for the carers. Although the services offered are of high quality, they do not suffice.

In October 2013, recognizing the magnitude of the issue, the Greek Minister of Health assigned a working group to develop a National Dementia Strategy. The group consisted of specialised doctors and other health professionals, caregivers, lawyers, health economists etc. In September 2014, after a consultation period with all the stakeholders involved, the group presented the Strategy including specific recommendations for the improvement of care pathways and coordination of social and medical care. The Strategy was approved by the Greek Parliament in March 2016.

To this moment the implementation of strategy has begun:
1. A national dementia registry is underway by the Greek National Health Service Organisation-funding available from the National Strategic Reference Framework 2014-2020.
2. A rating system to measure the burden of dementia on families is being developed by the National School of Public Health taking into account socioeconomic and family status, place of residence, access to health and social care services etc. This will be used by the State to accordingly establish financial benefits for persons with dementia and their carers.
3. Dementia Day Care Centers in collaboration with Municipalities throughout the country are being designed– funding available from the National Strategic Reference Framework 2014-2020

**SYMPOSIUM 12**

**Unconventional comorbidities associated with brain aging: A focus on depression and dementia**

**S12.2 | Separate and interactive associations of urban trauma and depression on brain structure: Implications for assessing depression in older adults**

**A. Karstens**  
University of Illinois, Chicago IL, USA

**Introduction:** Trauma and depression have each been associated with cognitive and brain structural alterations, but their combined effect on these outcomes is unclear. We investigated the separate and interactive associations of trauma and depression on cognition and brain aging in a sample of ethnically-diverse urban dwellers.

**Methods:** 284 adults aged 30-89 were divided into four groups based on current depression and trauma history. Individuals meeting DSM-IV criteria for a depressive disorder were considered Depressed (D+) and individuals rated as having a trauma history on a diagnostic interview were considered positive for Trauma (T+).

Resulting Ns were 73 D+T+, 56 D+T-, 68 D-T+, and 87 D-T-. Cognitive domains of VERBAL learning/free recall/recognition, VISUAL learning/free recall/recognition, and speeded attention/cognitive flexibility were assessed and cortical thickness and tractography derived structural connectomics were performed on T1/SPGR and diffusion tensor imaging collected in these same individuals.

**Results:** Multivariable linear regressions adjusting for age revealed that Trauma, regardless of Depression, was associated with worse VERBAL performance; driven by verbal list and prose passages learning and memory, but not recognition and most pronounced in older adults. Regression analyses adjusting for age
revealed an association between cortical thickness in the left prefrontal cortex (PFC) and Trauma; specifically the pars orbitalis, middle frontal and orbitofrontal regions. While left PFC cortical thickness did not mediate the association between Trauma and VERBAL performance, select subregions revealed lower efficiency metrics in connectome analyses that may explain these relationships.

**Conclusions:** Trauma, regardless of Depression, associated with worse verbal learning and memory performance but not recognition, particularly in older adults. Taken with neuroimaging findings, this suggests the retrieval problem seen with Trauma may be related to altered PFC network efficiency. Clinicians working with older adults in urban settings should query for trauma in addition to depression when considering subjective and objective measures of cognition.

**S12.3 | Impact of thyroid function on white matter connectivity: Implications for geriatric depression and antidepressant treatment response**

**O. Ajilore**

University of Illinois, Chicago IL, USA

**Introduction:** Previous studies from the basic neuroscience literature have suggested that thyroid hormone plays an important role in oligodendrocyte precursor differentiation/maturation and subsequent myelination. In geriatric depression, poor treatment response has been associated with white matter hyperintensity burden and microstructural white matter abnormalities. Given the use of T3 augmentation in the treatment of depression, the goal of the present study was to explore the association of thyroid-stimulating hormone (TSH) levels with diffusion tensor imaging (DTI) measures and the association of baseline TSH levels with antidepressant treatment response.

**Methods:** 164 subjects with TSH levels measured as part of a screening panel of labs for larger neuroimaging study were analyzed. Four tracts of interest, left and right uncinate fasciculus and left and right cingulate bundle, were virtually dissected from whole-brain tractography. Fractional anisotropy measures were obtained for all four bundles. 9 depressed subjects received 8-12 weeks of citalopram as part of pilot treatment study. Hamilton Rating Scales for Depression were obtained every two weeks until study completion. Partial correlations between variables of interest were calculated controlling for age, sex, and vascular risk factors.

**Results:** In the overall sample, TSH was significant correlated with FA in the right uncinate (r = -.23, p = .004, df = 151). This effect was driven by older males (r = -.342, p = .025, df = 41). TSH levels were strongly associated with treatment response, but the results were not statistically significant due to a small sample size (r = -.597, p = .21, df = 4).

**Conclusions:** Thyroid status is significantly related to white matter integrity in fiber bundles associated with mood. Baseline TSH levels may also predict treatment response. Further studies are needed to determine whether select older depressed patients with structural connectivity abnormalities might benefit from short-term T3 augmentation of antidepressant treatment.

**S12.4 | Late-life anxiety disorders, mood disorders, somatic symptoms and medical comorbidity**

**C.E. Gould**

Stanford University and the Palo Alto VA Health Care System, Palo Alto VA, USA
**Introduction:** Anxiety disorders co-occur with depression across the lifespan (Byers et al., 2010). In addition to comorbidity with depression, anxiety symptoms confer an increased risk of multimorbidity (Gould et al., accepted). Somatic symptoms may have an important role in understanding the extent to which medical comorbidity co-occurs with anxiety and depression. Here, we aimed to examine co-occurrence of somatic symptoms and somatic disorders with anxiety and mood disorders in an anxiety treatment-seeking sample.

**Methods:** Participants were studied as part of an ongoing pilot study examining a DVD-delivered treatment for late-life anxiety disorders. Participants were aged 60 years or older, free of cognitive impairment, and diagnosed with one of the following anxiety disorders: Generalized Anxiety Disorder, Social Anxiety Disorder, Anxiety Disorder Other Specified/Unspecified, Panic Disorder, or Agoraphobia. Trained interviewers used the Structured Clinical Interview for DSM-5 to make diagnoses. Additionally, participants completed measures of anxiety (Geriatric Anxiety Scale), somatic symptoms (Somatic Symptom Scale), depressive symptoms (Patient Health Questionnaire-9 item), and comorbidity (Comorbidity Questionnaire).

**Results:** Participants studied were 24 adults (M age = 68.08, SD = 6.66 years) with SCID-5 diagnosed anxiety disorders. Somatic symptom severity was strongly associated with both anxiety severity, \( r = .57, p = .005 \) and depressive severity, \( r = .46, p = .03 \). In the presentation, we also will describe patterns of co-occurring disorders with regards to anxiety disorders, depressive disorders, and Somatic Symptom Disorder and Illness Anxiety Disorder.

**Conclusions:** Findings suggest that somatic symptoms are strongly associated with both anxiety and depressive symptoms severity. Thus, the inclusion of somatic symptom disorders in the DSM-5 may increase detection and consideration of medical comorbidity in the context of psychiatric disorders. Further consideration of the role of somatic symptoms in anxiety and depression may illuminate underlying etiologies of these disorders in late life.

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**SYMPOSIUM 13**

**Diagnosis and intervention for neuroprogression in psychiatric disorders**

**S13.1 | Pathways and mechanisms contributing to neuroprogression in unipolar and bipolar disorder**

**M. Maes**
Department of Psychiatry, Deakin University, Geelong, Australia

Neuroprogression in depression and bipolar disorder refers to a) the clinical progression characteristic of neuro-psychiatric and neuro-cognitive disorders; and b) the neurological substrates of that progression, namely disorders in neuronal function (e.g. elevated neurotoxicity, lower neurogenesis and neuroplasticity) that are induced by activated immune-inflammatory and oxidative–nitrosative stress (O&NS) pathways. Exposure to depressive episodes (staging) may magnify the size of immune-inflammatory and autoimmune responses, possibly increasing the risk towards new depressive episodes. The aim of this talk is to review the immune, inflammatory, autoimmune and O&NS pathways that are thought to underpin neuroprogression in depression.
1. There are positive associations between the number of previous depressive episodes and immune-inflammatory biomarkers and serum neopterin, interleukin-1 and tumor necrosis factor-α. The neuroprogressive effects of these cytokines are discussed.
2. Recurrency of depression is associated with increased autoimmunity directed against serotonin (5-HT). Increased autoimmunity is associated with activated inflammatory pathways.
3. IgM-mediated autoimmune responses directed against oxidative specific epitopes (OSEs) are significantly increased in chronic depression. Chronic depression is also accompanied by increased IgM responses directed against nitroso-(NO) adducts indicating hypernitrosylation and increased natural autoimmunity against NO adducts. Both autoimmunity against OSEs and NO adducts may be major causes of neuroprogression and neurodegeneration.
4. Chronic physio-somatic (formerly called psychosomatic) symptoms in depression and pregnancy are associated with induction of the tryptophan catabolite (TRYCATs) pathway via activation of indoleamine 2,3-dioxygenase (IDO). Some of these TRYCATs, e.g. quinolinic acid and picolinic acid, have neurotoxic effects by increasing oxidative damage.
5. Depression, and in particular chronic depression, is also accompanied by leaky gut or increased gut permeability leading to increased levels of bacterial antigens and LPS in the circulation. This indicates increased bacterial translocation, which may drive immune-inflammatory pathways, activated O&NS pathways and autoimmune responses.
6. All the above pathways may activate the Toll-Like Receptor (TLR) Radical Cycle which may be a key component leading to chronic immune-inflammation and O&NS and thus neuroprogressive processes.

S13.2 | Inflammation-induced increase in glutamatergic activity contributes to neuroprogression in patients with mood disorders
E. Haroon
Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta GA, USA

Studies using a variety of disease models ranging from epilepsy to multiple sclerosis have consistently implicated increases in brain glutamate concentrations induced by acute or persistent inflammatory activation as a factor that can lead to kindling and neuroprogression. Using magnetic resonance spectroscopy (MRS), we had earlier demonstrated that inflammatory stimulation following 4-week administration of the cytokine interferon (IFN)-alpha for treatment of hepatitis c virus (HCV) disease resulted in robust increases in creatine normalized concentrations of glutamate (from baseline) in the basal ganglia and anterior cingulate regions, which in turn were associated with development of symptoms of depression including reduced motivation and psychomotor slowing. Aging and senescence are associated with increased proinflammatory activity, depression, cognitive impairment and neuroprogression. We hypothesized that older subjects would show more robust inflammatory activation following IFN-alpha compared to younger subjects paralleled by concomitant increases in brain glutamate concentrations. To test this hypotheses, we compared 8 older subjects (age > 55 years) to 9 younger subjects (age < 55 years) who received identical doses of IFN-alpha, and 7 older and 7 younger HCV controls who were not treated with IFN-alpha using a longitudinal pre-post (baseline - 4 week) paradigm. At four weeks, IFN-alpha induced greater increases in the concentrations of plasma soluble tumor necrosis factor receptor type 2 (sTNFR2 - a marker of inflammatory cytokine activity) in left basal ganglia regions of older compared to younger subjects and HCV controls. Intriguingly, the glutamate increases in the left basal ganglia were predicted by increases in the plasma concentrations of the cytokine tumor necrosis factor (TNF)-alpha only among older subjects - a relationship that remained significant after control of covariates. In addition, left basal glutamate increases were associated with decreased ability to
experience pleasure (anhedonia), prolonged reaction time (psychomotor slowing) and decreased psychomotor activity (psychomotor retardation), thus validating our hypotheses regarding the association between aging, inflammation and brain glutamate changes. Our subsequent study using patients with major depressive disorder not only yielded further validation of the association between inflammatory activation, basal ganglia glutamate increases and behavioral changes; but also pointed to the role played by inflammation-induced glial pathology in mediating these associations.

**S13.3 | Pharmacologic interventions to arrest neuroprogression**

**F. Boufidou**

Biopathology and Clinical Microbiology Laboratory, Eginiton Hospital, Athens, Greece

Inflammation seems to be a key-player in the complex interplay between the various aspects that contribute to the concept of neuroprogression in psychiatric disorders. In an attempt to identify the appropriate agent for arresting neuroprogression, the evaluation of anti-inflammatory drugs that have already been used for the benefit of psychiatric patients, besides conventional pharmacotherapy, is a reasonable approach. Clinical trials with adjunctive anti-inflammatory treatment in psychiatric disorders will be presented along with a brief overview of the literature about the potential utility of anti-inflammatory medication in psychiatry. This past experience will be discussed and information about the drugs that were used will be given. Side effects and considerations about possible implications on human homeostasis will also be discussed.

**S13.4 | Modulation of immune system activation may arrest neuroprogression in affective disorders**

**A. Halaris**

Department of Psychiatry, Loyola University Chicago Stritch School of Medicine, Maywood IL, USA

**Background:** A pro-inflammatory state in unipolar and bipolar disorder has been described in the literature. A few clinical studies have referred to the beneficial effects of add-on celecoxib, a COX-2 inhibitor, for a short period of time to reverse treatment resistance in unipolar depression. Although many pharmacological treatments exist for bipolar depression, none have included the use of a COX-2 inhibitor as adjunctive treatment option. Our study aimed to assess the outcome of treatment resistant bipolar depression following combined treatment of escitalopram plus celecoxib. We treated bipolar depressed patients, not previously fully responsive to antidepressant monotherapy, with escitalopram in combination with the anti-inflammatory agent, celecoxib. The primary hypothesis was that combination treatment will result in augmented treatment responses and a greater number of remitters compared to escitalopram monotherapy. Additionally, it was hypothesized that there would be an earlier response (earlier decline in HAM-D scores) in the escitalopram + celecoxib group vs. escitalopram alone. A secondary hypothesis was that there would be a reduction in pro-inflammatory biomarkers at end of treatment in patients randomized to receive the combination treatment.

**Methods:** This was a 10-week, randomized, double-blind, two-arm, placebo-controlled study. The study included a screening visit, a 1-week washout phase, a 1-week placebo run-in phase and an 8-week flexible dose phase. In addition to quantifying and qualifying symptoms of depression, we also considered the degree and intensity of perceived stress using the Perceived Stress Scale (PSS) before and after treatment.

**Results:** When comparing HAM-D mean scores pre and post treatment in the control group (escitalopram + placebo) vs. the active group (escitalopram + celecoxib), there was a statistically significant reduction in mean scores in the active group (p = 0.005), but not in the control group (p = 0.145). When comparing MADRS mean scores pre and post treatment in the control group vs. the active group, there was a
statistically significant reduction in mean scores in the active group (p <0.001), but not in the control group (p = 0.172). When comparing HAM-A mean scores pre and post treatment in the control group vs. the active group, there was a statistically significant reduction in mean scores in the active group (p = 0.047), but not in the control group (p = 0.756).

Discussion: Depressive symptoms, as measured by HAM-D and MADRS scales, when patients were treated with the combination escitalopram and celecoxib, improved with high statistical significance post treatment when compared to baseline, while those in the escitalopram group alone did not. Anxiety scores in the combination group also decreased post-treatment with statistical significance, while those in the escitalopram group alone did not. PSS scores decreased significantly in the combination group while those in the escitalopram group did not. We ruled out pain perception as a possible confounding factor. Reversal of treatment resistance depression by modulation of the inflammatory response may arrest neuroprogression of affective illness.

SYMPOSIUM 14
Dementia with Lewy Bodies (DLB)

S14.1 | Diagnosis and management of dementia with Lewy bodies in clinical services: Results from the DIAMOND-Lewy study
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Introduction: The aim of the "Improving the diagnosis and management of neurodegenerative dementia of Lewy body type in the United Kingdom National Health Service (NHS)" (DIAMOND-Lewy) programme, which comprises multiple work packages, is to improve patient management and clinical outcome through the development, and subsequent assessment, of an evidence-based LBD practical management toolkit for clinicians.
It has been estimated that only around one in 3 cases of DLB are currently detected in routine secondary care, despite the existence of validated diagnostic criteria. This component of the programme (Work Package 1A) includes a baseline assessment of DLB diagnosis and management in memory and dementia services within the NHS.

Methods: The research team screened consecutive consultations at nine memory/dementia services at sites in two areas, North East and Eastern England, over an 18 month period from January 2013. All contacts - initial assessment, review, ad hoc and emergency consultations were included. We conducted a retrospective review of clinical documentation in 70 patients with DLB and 70 non-DLB controls matched for age, gender and MMSE score, comparing time from presentation to diagnosis, and the extent and nature of pre- and post-diagnostic multidisciplinary input, as well as determining the prevalence of core, suggestive and supportive DLB features.

Results: Case notes of over 9 410 individual patients, of whom 52.4% had a diagnosis of dementia, were reviewed. Patients with DLB comprised 4.2% of all dementia cases, and 4.3% of incident cases. There was statistically significant variation between different services, with prevalence rates ranging between 1.8% and 5.9% for individual services. DLB was significantly more prevalent in men and in younger patients.
Conclusions: The prevalence and incidence of clinically diagnosed DLB in secondary care services remains lower than that observed in neuropathological studies and there is considerable variation in rates of diagnosis between individual services, despite the existence of validated diagnostic criteria. Reasons for this might include limited recognition of core and suggestive clinical features, difficulty in translating recent advances in DLB research into clinical practice, and possibly also real differences in prevalence of the disease. A brief assessment tool incorporating the range of DLB symptoms, such as scales for visual hallucinations and fluctuations, suitable for use in routine practice, may help address this.

S14.3 | The cognitive profile and associated symptoms of Lewy body MCI

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Background: Prodromal Alzheimer’s disease has been extensively studied, but relatively little is known about prodromal dementia with Lewy bodies (DLB). Previous research has suggested that DLB is likely to be preceded by nonamnestic mild cognitive impairment (MCI), whereas Alzheimer’s disease is more likely to be preceded by amnestic MCI. Symptoms associated with DLB, such as decreased sense of smell and autonomic dysfunction are known to occur in the prodromal phase of Parkinson’s disease, a closely related disorder.

The Newcastle LewyPro Study is an ongoing prospective study which aims to characterise the clinical and biomarker profile of prodromal DLB. We hypothesised that MCI subjects with core and suggestive diagnostic features of DLB would display the cognitive profile associated with DLB, as well as other symptoms known to be associated with Lewy body disease.

Methods: Patients with MCI and possible symptoms of Lewy body disease were recruited. Each patient had a comprehensive clinical and neuropsychological assessment and striatal dopaminergic ¹²³I-FP-CIT imaging.

Lewy body MCI (LB-MCI) was defined by the presence of core and suggestive diagnostic features of DLB (fluctuating cognition, parkinsonism, visual hallucinations, REM sleep behaviour disorder, neuroleptic sensitivity and abnormal ¹²³I-FP-CIT imaging). Subjects with two or more diagnostic features were categorised as LB-MCI. Subjects with no diagnostic features were categorised as ‘other MCI’. Subjects with one core or suggestive feature were classed as possible LB-MCI.

Results: Seventy-five patients were recruited. The most common diagnostic features were cognitive fluctuations (39%) and REM sleep behaviour disorder (33%). 39% of subjects had a positive ¹²³I-FP-CIT scan.

36 patients were classed as LB-MCI and 21 classed as other MCI. 18 patients were classed as possible LB-MCI and were excluded from further analysis.

Compared with the other MCI group, LB-MCI subjects had worse verbal fluency (FAS 26.6 v 34.8; p=0.02); worse attention and executive function (digit vigilance task number correct 29.6 v 32.8, p=0.02; choice reaction time number of errors 2.7 v 1.4, p=0.02) and worse visuospatial function (angle discrimination task 25.1 v 16.8, p=0.01). They approached having better memory (Rey delayed memory 3.8 v 2.5, p=0.09).

Subjects with LB-MCI had more depressive symptoms (Geriatric Depression Scale 4.5 v 2.4, p=0.02) and scored higher on the Neuropsychiatric Inventory (total score 13.7 v 5.1, p<0.01; distress score 7.6 v 2.4, p=0.01).
Subjects with LB-MCI were also more likely to report drooling (53% v 10%, p=0.001); weak voice (41% v 11%; p=0.02); apathy (47% v 19%, p=0.03) and errors in spatial perception (35% v 0%; p<0.01).

Conclusions: It is possible to identify patients with core and suggestive features of DLB during the MCI phase. LB-MCI subjects display the characteristic neuropsychological profile of impaired attention, executive function and visuospatial function seen in DLB, as well as other symptoms associated with Lewy body disease.

S14.4 | Exploring cognitive and attentional fluctuations in DLB: A multimodal perspective

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Fluctuations in attention and cognition (FC) in Lewy body dementia (LBD) are common, affecting up to 90% of patients. In FC there appears to be an interruption of awareness and attention which is often associated with transient episodes of confusion and communicative difficulties. Remission to near-normal cognitive function can occur spontaneously in the absence of clear environmental triggers suggesting that FC in LBD is internally driven.

Neuropsychological studies in DLB have noted deficits in attentional function ranging from simple processing speed through to complex attentional tasks requiring significant executive input. In addition, selective attention and the maintenance of vigilance are both impaired. Both FC and attentional deficits have major impact on activities of daily living and evidence suggests they are likely to have a significant role in the formation of the distressing visual hallucinations that frequently accompany LBD. However their aetiology is not well understood but this is beginning to be addressed by the use of neuroimaging and other approaches.

In my presentation I will discuss highlight findings from spatial covariance network analyses applied to data derived from single photon emission computed tomography (SPECT) HMPAO brain imaging in LBD patients a spatially distributed network which encompasses both motor and parietal areas that associates with poorer cognitive function, increased FC and worse attentional function as measured both clinically and physiologically. These findings suggest indicate that FC and certain aspects of attentional dysfunction in DLB may, in part, depend upon both distributed motor and non-motor networks.

I will also describe data from functional magnetic resonance blood oxygen level dependent imaging (fMRI-BOLD) during an attentional-executive task. I will show that in addition to a specific behavioural attention-executive impairment in LBD patients, the distributed functional BOLD activity is different in LBD compared to Alzheimer’s disease patients with inefficiencies in neural processing particularly within attentional networks. These data will be complemented and supported by task based findings made from high density electroencephalography data collected in the same participants as well as functional connectome findings from resting state fMRI-BOLD studies.

Overall I will present arguments to suggest that attentional dysfunction and cognitive fluctuations in LBD are both the result of specific nodal deficits as well as global neural inefficiencies.
SYMPOSIUM 15
EEG manifested brain functional states and intra-individual variance of subjective experience

S15.1 | Dissociated EEG brain functional states in first episode productive schizophrenics
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We present and discuss the results of two EEG studies in first episode, neuroleptic naïve productive schizophrenic patients. The studies differ in the experimental design and the method used to analyze the EEG. Based on the proposals of an integrative model of the brain functions that create autobiography (M.Koukkou and D. Lehmann Brit J of Psychiat. 1983 142:221-231) the hypothesis was tested that:

a) The EEG manifested brain functional states represent in the ontogenetic domain the level of attained complexity of the cortico-cortical connectivity (the neuronal networks that represent autobiographical memory) and in the short-term temporal domain, the level of the momentary excitability of the working memory contents.

b) Dissociated organization and reorganization of the working memory contents underlie the pathophysiology of productive schizophrenic symptoms.

Study I: By schizophrenics , as defined above, age matched controls and three age groups of adolescents 19 channel EEG was recorded and analyzed (FFT) during resting and after the presentation of verbal stimuli. The centroid frequencies (HZ) of the delta-theta, alpha and beta spectral frequency bands were computed as measure of the momentary activated neuronal networks.

Results: Schizophrenics compared with all other groups showed in resting lower delta-theta centroids and higher alpha and beta centroids. After verbal stimuli showed similarities in delta-theta and beta centroids with the two younger groups of adolescents and in alpha centroids similarities with the older groups of adolescents (Koukkou M.1982 Psychiatry Research 6: 235-244).

Study II: In another group of schizophrenic patients as defined above the19-electrode EEG was recorded in resting and the momentary electric field configurations were estimated into sequences of momentary maps. The map series were assigned to four individual microstate classes and tested for differences between schizophrenics and controls (Koenig Th. et al 1999 Eur Arch of Psychiatry and Clin. Neurosci 249:205-211).

Results: One microstate class displayed significant different field configurations and shorter durations in patients as compared with the matched controls.

In a multicenter study (D. Lehmann et. all, 2005: Psychiatry Research Neuroimaging 138:141-156) patient's microstates differed in duration, frequency and field configurations from matched controls.

Discussion: Interpreted within the framework of our model the results indicate deviations in organization and reorganization of the working –memory contents (the neuronal networks) during productive schizophrenic symptomatic. They support the hypothesis of task- and age –dissociated brain functional states in productive schizophrenic symptoms.
Modalities of thinking refer to mental representations of thought content. Three modes are frequently distinguished: spatial visualization, object visualization, and verbalization. They refer to the mental creation of low-resolution, spatial images, the creation of detailed, realistic visual images, and internal speaking, respectively. Previous studies suggest that different mental representations are reflected by brain electric activity in different functional brain networks. Based on electroencephalography (EEG) data, brain networks can be identified via independent component analysis (ICA). Beyond metabolic networks derived from functional magnetic resonance imaging, EEG-derived networks allow the discrimination between brain electric activity in different EEG frequency ranges. Via EEG source localization, the cortical location of network components can be identified at agreeable spatial resolution. The present study investigated state and trait effects of modalities of thinking on activity in EEG source-localized ICA-derived brain networks.

From 61 male, right-handed students, we obtained 64-channel EEG and modality-related person parameters. Recordings were conducted during four conditions: spatial visualization, object visualization, verbalization, and resting. For each condition, EEG data were source-localized with exact low resolution electromagnetic tomography (eLORETA) and ICA was applied to identify cross-frequency functional independent networks across 6 frequency bands (delta to beta-2). Visual-verbal cognitive style questionnaires were used to assess an individual’s habit to represent information in the three different modalities. Effects of condition and style on activity in cross-frequency functional brain networks were evaluated via repeated-measures MANOVAs, post-hoc univariate ANOVAs, paired t-tests, Pearson correlations, and path modelling.

Statistics identified four task-dependent and three style-related functional brain networks. All task-dependent networks were characterized by decreases in alpha activity in modality-specific pathways. All style-related networks were characterized by increases in alpha activity in modality-specific pathways. Furthermore, all networks were associated with opposing alpha changes in pathways of other modalities.

Our results suggest that modality-related tasks can induce short-term changes in activity of modality-specific brain networks. These changes might reflect decreased inhibition in areas necessary to successfully pursue the task (e.g. increased alpha in the spatial visual stream during visualization), as well as increased inhibition in areas not necessary to pursue the task (e.g. decreased alpha in sensory-motor areas during visualization). These antagonistic effects may prevent intruding effects of modality-irrelevant processing. Moreover, visual-verbal cognitive style may induce long-term changes in activity of modality-specific brain networks. The respective changes suggest increased neural efficiency of brain areas frequently applied (e.g. decreased alpha in the spatial-visual stream by spatial visualizers). Longitudinal studies are needed to shed more light on the causality of the observed interrelationships between modality of thinking style and brain network processing.
The microstates of meditation: An EEG analysis

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Two phases of Transcendental Meditation (TM) – transcending and undirected mentation – were compared to each other and to task-free resting. Multi-channel EEG was recorded from 20 TM practitioners. Four classes of microstates were identified using an EEG microstate analysis. They were labeled A, B, C and D, based on their similarity to previously published microstate classes. For each class of microstates, the parameters mean duration, coverage, and occurrence were computed. Both, resting and transcending differed from undirected mentation with decreased prominence of Class A and increased prominence of Class D microstates. In comparison to undirected mentation, transcending additionally showed decreased prominence of Class C microstates. Based on previous findings on the functional significance of the microstate classes, the results suggest an increased reference to reality and decreased visualization during resting and transcending compared to undirected mentation. In addition, saliency of internally generated mentations was decreased during transcending compared to undirected mentation. This possibly reflects a decreased effort in attentional processing during transcending. It is proposed that the continuous cycling through these two phases of meditation during a TM session might facilitate and train the flexible modulation of the parameters of these microstates of these particular classes which are known to be altered in psychiatric disorders. This possibly promotes beneficial stabilizing effects for the practitioner of TM.

The Lifestyle for Brain Health (LIBRA) index: Validation studies of a new tool for dementia prevention

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Background: Dementia is a global public health problem. Identifying major determinants for dementia is important for understanding disease mechanisms and designing effective preventive strategies in the absence of curative treatment. Several factors have been identified that contribute to the risk for dementia, with most of the net effect being attributable to non-modifiable factors such as age, education and APOE genotype. Although being of predictive value, such information is of limited utility from a public health perspective in which it is more important to calculate someone’s “prevention fraction”. Recently, we therefore developed the ‘Lifestyle for Brain Health’ (LIBRA) score as part of the European (FP7) INnovative, Midlife INtervention for Dementia Deterrence (In-MINDD) project based on a multi-method approach. We validated the index in several population-based datasets.

Methods: Risk factors were identified by means of a systematic literature review and online-Delphi consensus study. From the literature, we extracted factors, their number of studies and effect consistency.
The results were presented to a group of eight dementia experts from different countries, who confirmed their importance for dementia prevention. A weight was then assigned to each factor based on their risk estimate as reported in meta-analyses, and these were summed up to yield a final score: the LIBRA score. Whether individual LIBRA scores predicted risk for dementia or incident cognitive impairment was then tested in several cohort studies including the Maastricht Ageing Study (MAAS).

**Results:** Out of 291 relevant articles, twelve factors were deemed most important after triangulation (review and expert consensus): physical inactivity, smoking, low-to-moderate alcohol use, cognitive activity, healthy diet, depression, hypertension, obesity, diabetes, hypercholesterolemia, coronary heart disease, and renal disease. Higher LIBRA scores did predict future dementia risk, especially in midlife and late life. These effects were independent of age, gender and education.

**Conclusion:** The LIBRA score could be a promising tool for quantifying an individual’s potential for prevention of dementia. Individual reductions in the LIBRA score could also be a new proxy outcome for trial success given the long latent period for the dementia outcome, but further validation in different dataset is welcomed.

**S16.2 | Sleep duration and the risk of incident cognitive impairment among white and non-white elderly Brazilians: 14-year follow-up of the Bambuí Cohort Study, Brazil**

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This study investigates the association of sleep duration with risk of incident cognitive impairment among white and non-white elderly Brazilians using data from a 14-year population-based cohort study and applying a multivariable competing risk regression with date of death as a competing risk event. Of the 1,606 subjects in the cohort, complete data on all study variables were available for 1,437 (89.5%). At baseline, 343 subjects had cognitive impairment and were excluded from the current analysis that comprised 1094 participants.

In multivariable analysis controlling for measures of sociodemographic, lifestyle, health status and African ancestry: non-white, who slept less than 6 h/night (SHR: 0.49; 95% CI: 0.29-0.83) or between 6-6.99 h/night (SHR: 0.53; 95% CI: 0.33-0.88) were found to be at less risk of incident cognitive impairment than those who slept 7 to 7.99 h/night. For white participants, no statistically risk of incident cognitive impairment was found for those who slept less than 6 h/night (SHR: 0.81; 95% CI: 0.50-1.31); or slept between 6-6.99 h/night (SHR: 1.33; 95% CI: 0.91-1.95), when compared to those who slept 7 to 7.99 h/night.

In this elderly Brazilian population, white and non-white Brazilians are characteristically different regarding the association of sleep duration to incident cognitive impairment.

**S16.4 | From possibility to action: Translating epidemiological findings into the real world**

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While the absolute number of people with dementia is expected to triple over the next decades, prevalence and incidence rates appear to have declined over the last 20 years. Lifestyle changes and
better disease risk management and treatment might be responsible for this, at least partly. Recent research has identified a number of modifiable risk and protective factors that could be suitable targets for primary dementia prevention. Novel candidate risk factors have emerged, too, but need further validation. While these are promising advances, evidence from randomized clinical trials is still limited and suggests more modest effects. In this presentation, several challenges will be discussed that exist for implementing current findings into public health and the real-life context of people. The findings from this session’s speakers will be highlighted as to show some new directions for additional prevention targets, intelligent participant selection and outcome monitoring. Recent findings from past prevention trials will be reviewed, including the largely negative European In-MINDD feasibility study, and the new project ‘MijnBreincoach’ will be presented.

**SYMPOSIUM 17**

**Eating disorders and the brain**

**S17.1 | Set shifting and moral reasoning in anorexia nervosa**

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Moral reasoning is defined as the cognitive process by which the individual draws conclusions, which often exceed the available information. There are two basic types of reasoning: inductive reasoning and deductive reasoning. Reasoning problem solving has been the subject of research interest in the past, with different approaches. Two reasoning systems have been proposed: the first system (heuristic system) tends to solve problems based on prior knowledge and beliefs using fast and automatic processes, while the second system (analytic system) is involved in the reasoning process based on logical rules. The reasoning process in humans is characterized by the interaction between the two systems.

A fundamental question is whether psychopathology symptoms and / or personality traits are involved in reasoning process and have an impact on reasoning performance. There are findings that suggest extroversion / introversion fluctuations may have an adverse effect on reasoning performance. Studies have investigated deductive reasoning in mood disorders or psychopathology with strong emotional traits. Other studies have evaluated reasoning process in anxiety disorders and have identified separately reasoning patterns associated with threat. However, there is limited research data on the impact of affective variables in reasoning process. Moreover, significant differences have emerged in reasoning of individuals with OCD according to the neutral / emotional content of reflections. In this context, there are no available research data on reasoning process in patients with eating disorders.

The cognitive flexibility (cognitive flexibility, mental set shifting, task switching / shifting) can be defined as the mental capacity exchange of thought between two different concepts and the ability of the individual to think multiple concepts simultaneously. Impaired cognitive flexibility has been found in neuropsychiatric disorders such as anorexia nervosa, obsessive compulsive disorder, schizophrenia and autism. Typically, patients with eating disorders often have rigid attitudes on issues related to food and have difficulties solving problems with alternatives. Impaired cognitive flexibility is considered as an important risk and maintenance factor for anorexia nervosa. Studies have shown poor cognitive flexibility in patients with anorexia nervosa, and recovered patients show reduced cognitive flexibility compared to healthy
individuals. Furthermore, reduced cognitive flexibility has been associated with longer duration of disease, and more pronounced rituals in anorexia.

**S17.2 | The interplay between symptomatology and neuroimaging findings in anorexia nervosa**

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Anorexia nervosa is characterized by the maintenance of an undernourished, or starved, state. Persistent restrictive eating, or the recurrent intake of a diet that is inadequate to sustain a healthy weight, is the central behavior maintaining AN. While a range of neural disturbances have been reported in AN, abnormalities in systems relevant to reward processing and the development of habit systems have been consistently described in both structural and functional neuroimaging studies. Functional, molecular and genetic neuroimaging has highlighted the existence of brain anomalies and neural vulnerability factors related to anorexia nervosa. Brain research on gray matter (GM) and white matter (WM) volumes had been inconsistent, possibly due to the effects of acute starvation, exercise, medication, and comorbidity, but newer studies have controlled for such effects. Those studies suggest larger left medial orbitofrontal gyrus rectus volume in ill adult and adolescent anorexia nervosa after recovery from anorexia nervosa. The orbitofrontal cortex is important in terminating food intake, and altered function could contribute to self-starvation. The right insula, which processes taste but also interoception, was enlarged in ill adult and adolescent anorexia nervosa, as well as adults recovered from the illness. The fixed perception of being fat in anorexia nervosa could be related to altered insula function. A few studies investigated WM integrity, with the most consistent finding of reduced fornix integrity in anorexia nervosa—a limbic pathway that is important in emotion but also food intake regulation. Functional brain imaging using basic sweet taste stimuli in eating disorders during the ill state or after recovery implicated repeatedly reward pathways, including insula and striatum. Brain imaging that targeted dopamine-related brain activity using taste-reward conditioning tasks suggested that this circuitry is hypersensitive in anorexia nervosa. Those results are in line with basic research and suggest adaptive reward system changes in the human brain in response to extremes of food intake-changes that could interfere with normalization of eating behavior.

**References:**


**SYMPOSIUM 18**

**Late-life depression: Cognitive, molecular basis and neural networks**

**S18.1 | Molecular and neural basis of late-life depression – Insights from animal study**

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Background: Late life depression (LLD) is a serious clinical disorder, whose symptoms differ from depression earlier in life, suggesting that the underlying mechanisms are also different. The present study used two mouse models of induced depression, providing translational models of two factors that are common in the elderly and may interact and contribute to the development of LLD. The chronic stress (CS) model mimics everyday life stressors, and bilateral carotid artery stenosis (BICAS) provides a model for vascular insufficiency (VI) that is known to induce damage to the deep white matter. Exposing old and young female mice to these procedures followed by an extensive behavioral test battery, enabled us to test the hypothesis that old female mice are more susceptible to the hazardous effects of stress and VI.

Methods: CS: Mice were exposed to CS or control conditions for 5 weeks, after which they underwent extensive behavioral testing while continuing exposure to CS. VI: Common artery stenosis was induced using bilateral implantation of metal coils around the carotid arteries. As LLD is characterized by cognitive symptoms and residual cognitive impairment, the effects of chronic stress and vascular insufficiency on neuroplasticity, mainly manifested by neurogenesis, glial activation, and BDNF levels, were tested.

Results: Old female mice were more vulnerable to the effects of chronic stress on weight than young mice. Two way ANOVA with repeated measures comparing change in body weight from baseline until after eight consecutive weeks of CS revealed a significant triple interaction of time, age, and exposure to CS (F[1,58] = 7.221, p<0.05) suggesting that only old mice exposed to CS significantly lost weight. Age by exposure interaction was demonstrated in the two cognitive tests used - NOR (F[1,76]=4.373, p<0.05) and radial-arm water maze (RAWM) (F[1,74]=4.107, p<0.05), indicating that the cognitive functioning of young mice exposed to CS was higher compared to old CS mice. Age by exposure interaction was also demonstrated in the elevated plus maze (EPM) test (F[1,74] = 3.975, p<0.05), indicating that CS increased the amount of time young mice spent in the open arms. White matter lesions following BICAS were demonstrated histologically using myelin basic protein staining. The effect was more pronounced in old mice. Triple interaction of time, age and treatment (F[1,27]=6.852, p<0.05) in the SIH test indicated blunted response of old VI mice to acute stress. Old VI mice also displayed longer RAWM latencies compared with young VI mice (age by treatment interaction F[1,29] = 7.318 p<0.05). Old mice also displayed lower levels of neurogenesis reflected by lower levels of doublecortin (F[df 1,12] = 120.45 p<0.0001) and synapsin (F [1,11] = 5.068, p<0.05).

Conclusions: Chronic stress and vascular insufficiency, common precipitating factors for depression, anxiety, and cognitive decline, have differential effects depending on age. While old mice were susceptible in terms of developing behavioral and cognitive features often associated with LLD, young mice displayed striking resilience in both models. Such findings have key implications for a better understanding of debilitating symptoms that commonly occur in elderly individuals as well as their prevention and treatment.

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SYMPOSIUM 19
Sex differences in preclinical neuropsychopharmacology

S19.2 | Psychotropic actions of aromatase inhibitors: Preclinical and clinical data
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Aromatase inhibitors, which are widely used in the clinic for the treatment of estrogen-dependent cancers, have been associated with psychiatric effects ranging from mania to depression. In studies at the Dep. of Pharmacology, Medical School, University of Athens, we have investigated whether subacute letrozole treatment has an effect in the forced swim test (FST), which is a test of antidepressant potential in cycling female rats. Females were treated with either vehicle or the antidepressant fluoxetine for 28 days, in combination with subacute letrozole (3 injections in 24 hours) or sustained (7 days, 1 injection/day) letrozole treatment. Behavioral response in the FST was evaluated with the use of the software Kinoscope. Also, gonadal hormone levels were assayed following behavioral testing. Immobility duration in the FST was reduced following acute aromatase inhibition, indicating letrozole’s antidepressant potential. Additionally, swimming duration was enhanced, suggesting letrozole’s action on the serotonergic system. Instead, aromatase inhibition for one week did not show an antidepressant response. Moreover, serum testosterone levels were elevated following acute letrozole treatment and this was associated with the decreased depressive behavior in the FST. On the other hand, the regression analysis revealed that progesterone levels explained the increased swimming behavior in the FST.

In other experiments, we have investigated the role of estrogens, locally synthesized in the brain by the enzyme aromatase. FST was performed 4 weeks after gonadectomy of female and male rats, in order to eliminate gonadal hormone secretion. Before the FST, rats were injected, i.p. for one week, with either vehicle or the aromatase inhibitor letrozole (1 mg/kg). Aromatase activity in the hypothalamus was determined by the production of tritiated water associated with the conversion of [1β-3H]-androstenedione into estrone and verified that letrozole inhibited aromatase in the brain. In the open field test, females were overall more active and explorative than males, whereas gonadectomy eliminated this sex difference. Aromatase inhibition had no effect in the open field test. In the FST, females exhibited overall higher immobility and lower swimming duration than males. Interestingly, letrozole tended to enhance immobility in gonadectomized male and female rats, in comparison to sham-operated rats; a finding indicative of enhanced depressive symptomatology in rats lacking chronically both peripheral- and brain-derived estrogens. Moreover, neurochemical analysis showed that aromatase inhibition decreased noradrenaline levels and dopaminergic ratios in the hippocampus and prefrontal cortex of male and female rats, irrespectively of gonadectomy. Interestingly, letrozole enhanced the serotonergic ratio, only in castrated male rats.

These findings indicate that aromatase inhibitors have psychotropic attributes that depend on treatment duration. Therefore, in an ongoing human study, we investigate whether aromatase inhibitors have differential mood effects after acute or chronic treatment. In order to assess this, we perform a detailed psychiatric evaluation of oncology patients (women with breast cancer) treated with aromatase inhibitors in three Greek hospitals. The psychiatric evaluation is performed with the use of psychiatric scales, such as the HADS-A and HADS-D, as well as the Athenian Insomnia Scale.

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S19.3 | Brain vulnerability to Alzheimer’s disease pathology: Does sex matter? 
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Despite the considerable progress in the understanding of pathophysiology of neurodegenerative disorders over the last three decades, Alzheimer’s disease (AD) remain a complex and devastating disorder affecting more than 40 million people worldwide. While the importance of Tau-mediated neurodegeneration in AD is well established, the interplay of different risk factors for the disease (e.g. aging, mutations, environmental parameters and sex) is poorly understood. Specifically, women are more prone to AD than men but still the biological mechanisms underlying such sex differences in AD incidence...
as well as vulnerability to stressful conditions remain unclear. Consistent with suggestions that lifetime stress may be an important precipitating factor of AD pathology, we have previously showed that chronic stress and the main stress hormones, glucocorticoids (GC), trigger Tau accumulation and aggregation \(^1,2\). However, the molecular mechanisms through which stress/GC and sex facilitates Tau aggregation pathology remain unclear. Using both animal and cellular models of Tau pathology expressing the most common human mutation of Tau, P301L, our studies reveal sex-specific spatial reference memory impairments, with transgenic female animals being more vulnerable to the deleterious effects of stress. This behavioural phenotype was associated to stress-increased Tau aggregation through deregulation of the chaperone machinery e.g. Hsp90 molecular chaperones. In addition, an increased generation of truncated Tau and activation of apoptotic pathways were found in the hippocampus of stressed transgenic female mice leading to neurodegeneration and cell death \(^3\). Further molecular analysis showed that chronic stress induced an mTOR-dependent blockage of autophagy clearance machinery, decreasing LC3II and increasing p62 protein levels in P301L-mice. In addition, we found that chronic stress triggers the formation of Stress granules (SGs), a neurodegenerative mechanism that is recently suggested to trigger Tau aggregation. As GC are responsible for many detrimental effects of chronic stress and thus, often used to clarify the stress molecular “signatures”, we next treated P301L-Tau-expressing SHSY5Y cells with the synthetic glucocorticoid, Dexamethasone (DEX). Providing further support of the above in vivo results, our in vitro findings show that DEX mimicked the stress-evoked blockage of autophagy and inductions of SGs leading to Tau accumulation and related cell death in this AD cellular model. Moreover, co-treatment with CCI-779 (Temsirolimus), an established stimulator of autophagy, attenuated the aforementioned DEX-driven mechanisms of neurodegeneration. Altogether, these findings contribute to unravel the molecular mechanisms underlying the stress-triggered Tau pathology and the interplay between clinically relevant precipitating factors, such as sex and stress, highlighting novel precipitating targets of Alzheimer’s disease neuropathology and vulnerability.

References:

S19.4 | Neuroplasticity modulation: Effects of stress, gender and antidepressants

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Recent theories link psychiatric disorders, such as as anxiety and depression with neuroplasticity and neurochemical changes. These effects include sex differences in the serotonergic activity, spine density, dendrite length and adult neurogenesis in brain regions related to stress and emotion, such as the hippocampus and the prefrontal cortex. Herein, we provide novel and previous evidence from our group showing sex differences in the vulnerability of different brain areas and circuits in models of stress and depression. Our findings show that depressive-like symptomatology in the forced swim test (FST) is more evident in females than in males, accompanied by decreased serotonergic turnover ratio in the female hippocampus. Similar findings are obtained with the CMS model of depression, where females exhibit
reduced serotonergic activity in the hippocampus. Furthermore, in the learned helplessness model pronounced sex differences in the manifestation of behavior exist and consequently sex differences in adult hippocampal neurogenesis are also evident. Lesion and inactivation studies have also shown that the integrity of the circuit hippocampus-prefrontal cortex (PFC) is necessary for the expression of passive (depressive) behaviors in the FST in both sexes. However, when this circuit is disrupted sertraline lacks an antidepressant effect only in males. This latter finding can be attributed to sex differences in basal levels of FST behavior. Moreover, when nucleus reuniens (RE) is lesioned, male rats do not exhibit a reduction in anhedonic behavior, evident as decreased sucrose intake. Also, the CMS-induced alterations in neuroplasticity indices, such as decreased spine density and dendritic neuronal length in the PFC and the hippocampus are prevented in lesioned male rats. Our findings uncover that the communication of PFC and hippocampus, depending on RE, is required for the appearance of depressive-like behavior in both sexes. Moreover, they highlight the need of inclusion of both male and female animals in preclinical research for depression and other psychiatric disorders.

**SYMPOSIUM 20**

**CSF biomarkers in dementia**

**S20.1 | Classical biomarkers: Which question they do answer?**

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Classical CSF biomarkers, namely tau and phospho-tau proteins and amyloid peptide Aβ42, are useful in the (differential) diagnosis of dementia and they are now included in many internationally accepted guidelines. High CSF concentration of tau and phospho-tau proteins and low concentration of Aβ42 are highly suggestive of the presence of Alzheimer’s disease (AD) pathology, while normal values of all three biomarkers are highly suggestive of the absence of AD. Sensitivity and specificity are both high for the discrimination of AD from normal ageing, exceeding 85%. For the discrimination of AD from various psychiatric disorders including depression (pseudo-dementia) or alcohol-related cognitive disorders, sensitivity and specificity may approach 90% and may be even higher when combinations of the above markers are used, such as the tau/Aβ42 or phospho-tau/Ab42 ratio. For the differential diagnosis of AD from pure vascular dementia sensitivity and specificity are at least at the level of 85%. For the differential diagnosis from Dementia with Lewy Bodies of Frontotemporal Dementia, the discrimination may not be so good, but biomarkers may still be useful in many cases including patients with primary progressive aphasia or corticobasal syndrome. Preferably, all 3 classical biomarkers should be determined together, but they should not be used as a stand-alone diagnostic tool. They should be interpreted together with clinical, neuropsychological and imaging data. In the appropriate clinical setting, abnormal levels of all 3 biomarkers may increase the diagnostic confidence for the presence of AD, by at least 20–25%.

**S20.2 | Novel biomarkers (a-syn, TDP 43). Are they helpful?**

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Parkinsonian syndromes including Parkinson's disease (PD) and the atypical disorders are progressive neurodegenerative diseases that are characterized by slowness of initiation, movement and thought,
resting tremor and extrapyramidal rigidity. To date, the diagnosis of these diseases is based on the evaluation of the clinical symptoms of the patient from the neurologist. Due to the expanding phenotypical spectrum of atypical parkinsonian conditions, diagnosis is considered challenging, especially in early stages of disease. As such, the discovery and establishment of specific biomarkers that will allow early and/or differential diagnosis with a high degree of specificity has become an urgent necessity. To this end, we and others have tried to correlate the concentration of α-synuclein in blood plasma or CSF with the clinical manifestations of the patient, the diagnosis and the staging of disease. α-synuclein is strongly linked with PD pathology since aggregated α-synuclein species accumulate in filamentous structures known as Lewy bodies and Lewy neuritis. In addition, several missense mutations and gene multiplications in the gene encoding for α-synuclein have been associated with the familial forms of PD. In order to evaluate the possibility of α-synuclein to be used as a biomarker for PD and other related neurological conditions, we have developed an ultra-sensitive ELISA assay that allows the accurate quantification of α-synuclein concentration in all the biological fluids. Except from the high sensitivity, the methodology is highly selective and reproducible in a lower time of analysis. Using this assay, we have analyzed a great number of clinical samples (plasma, serum and CSF) of parkinsonian patients and healthy subjects. In these measurements, we have also applied the recently established pre-analytical procedures. In a parallel line of research, frontotemporal dementia is also difficult to be diagnosed since the symptoms of the disease, such as changes in the personality and behavior, difficulty in speech and movement, greatly overlap with other neurological conditions. To this end, our group is currently trying to develop a new method for the measurement of TDP-43 in order to investigate whether this protein can be used as a biomarker for this disease.

**S20.3 | Biomarkers in subcortical vascular dementia**

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Vascular dementia is a heterogeneous entity with multiple aetiologies, all linked to an underlying cerebral vascular disease. Large vessel strokes, small vessel disease, haemorrhagic insults, genetically determined arteriopathies, may give rise to vascular cognitive impairment (VCI), which also includes milder forms of cognitive impairment, often running under-unrecognized, especially in the elderly.

Among various subtypes, VCI related to subcortical small vessel disease (SSVD) is emerging as a common, fairly homogeneous subtype (VCI-SSVD). Its progressive course raises the need for adequate diagnostic and therapeutic interventions. Additionally it may appear with and without Alzheimer’s disease (AD) pathology. The clinical phenotype of the combined pathologies is often known as mixed type dementia. The overlap of SSVD, AD and normal aging makes the underlying clinical diagnosis challenging, thus requiring the use of biomarkers.

Markers from multiple sources, including blood, imaging, neuropsychological testing and cerebrospinal fluid (CSF), have been studied as possible surrogate markers of VCI-SSVD. A large number of them, mostly derived from CSF and blood have been investigated, although the studies have been small and the findings need to be replicated. However, several of these neurochemical markers have shown promise in separating VCI-SSVD from other subtypes of VCI and from AD. The most promising relate to the underlying pathophysiology of SSVD, which is associated with disruption of the blood-CSF/blood-brain barrier (BCB/BBB) and breakdown of white matter myelinated fibres and extracellular matrix, as well as inflammation in blood and brain.
Thus, the leading biomarker candidates are: (a) elevated CSF/blood albumin ratio, which reflects BCB/BBB disruption; (b) altered matrix metalloproteinases in CSF, reflecting extracellular matrix breakdown; and (c) various inflammatory cytokines and adhesion molecules in the blood. These changes are in contrast to the CSF alterations of amyloid beta peptide, phosphorylated and total tau, that characterize patients with AD.

Combining SSVD and AD biomarkers provides a powerful tool to a more precise diagnosis, management and identification of more homogeneous populations suitable for clinical trials. Thereby, biomarkers might promote therapeutic progress not only in VCI-SSVD, but also in AD.

**SYMPOSIUM 21**

**Neuroimaging in Dementia with Lewy Bodies (DLB)**

**S21.1 | Clinical correlates of amyloid deposition in dementia with Lewy bodies**

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**Background:** The pathological hallmarks of dementia with Lewy bodies (DLB) are Lewy bodies and Lewy neurites. Many cases of DLB also display amyloid-beta deposition, though it is unclear if this has any effect on the type or severity of symptoms that the person experiences. Amyloid PET imaging enables us to investigate this relationship in vivo.

The aim of this study was to investigate the relationship between brain amyloid deposition and clinical phenotype in DLB. We hypothesised that amyloid deposition in DLB would be associated with a phenotype with similarities to AD, such as greater memory impairment.

**Methods:** DLB (n=37), Alzheimer’s disease (n=20) and control (n=20) volunteers had an amyloid PET-CT scan using ¹⁸F-Florbetapir (Avid (Lilly)) and, where possible, an MRI (all but 7 cases). Each volunteer also had a clinical assessment including tests of cognitive function (Addenbrooke’s Cognitive Examination Revised (ACE-R), Rey Auditory Verbal Learning Test (AVLT), Trails A and B, FAS verbal fluency, computerised tests of reaction times, attention and visuospatial function); level of functional impairment (Bristol and Instrumental Activities of Daily Living scales) and symptom pattern and severity (Neuropsychiatric Inventory, cognitive fluctuations scales).

Amyloid PET scans were visually rated as amyloid positive or negative according to the manufacturer’s protocol. A region of interest analysis was performed using co-registered MRI scans to obtain standardised uptake value ratios in parietal, frontal, temporal, cingulate, occipital and striatal regions relative to a whole cerebellum reference region. Mean cortical deposition was calculated using an unweighted mean of parietal, frontal, temporal and cingulate regions.

**Results:** 54% of DLB cases had positive amyloid PET scans on visual rating. This was greater than controls (20%, p=0.01) but less than AD (85%, p=0.02). Mean cortical amyloid deposition in DLB was intermediate between AD and controls, though it was not significantly different to either group. DLB cases had higher occipital deposition compared with controls (1.20±0.18 v 1.08±0.12, p=0.04), but there were no other statistically significant differences between DLB cases and AD cases or controls in any region. Amyloid deposition was significantly higher in AD than controls in every cortical region.
There were no significant differences between amyloid positive and amyloid negative DLB cases in age (amyloid positive DLB 76.3±7.3 v 75.7±5.6 amyloid negative DLB, p=0.78), overall cognitive impairment (Addenbrooke’s Cognitive Examination: 64.9±16.5 v 61.9±13.3, p=0.29), level of functional impairment (Bristol ADL: 18.6±13.2 v 18.8±12.9, p=0.89), or any other clinical or cognitive scale, including measures of memory function (ACE-R memory domain: 13.2±6.0 v 13.1±4.8, p=0.96; Rey AVLT delayed memory: 1.7±2.4 v 2.2±2.7, p=0.42).

Conclusions: In keeping with previous studies we found that significant amyloid deposition is more common in DLB than controls, but less common than in AD. The pathophysiological significance of this remains unclear, as those with significant amyloid deposition did not show any phenotypical difference to those without amyloid deposition. Longitudinal follow-up of this cohort will determine whether amyloid deposition is associated with differences in disease progression.

S21.2 | Neuropathological validation of FP-CIT imaging

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Introduction: Dementia is increasingly recognised as a major health concern and accurate and earlier diagnosis of dementia and its subtypes is a high priority for health systems around the world. DLB is a major dementia subtype, being the second commonest neurodegenerative cause of dementia. Like Parkinson’s disease DLB is caused by synuclein pathology. Dopaminergic neurones in the substantia nigra pars compacta project to the striatum (the nigrostriatal pathway) and their loss is associated with the presence of α-synuclein pathology. This loss can be identified using dopaminergic imaging and such neuroimaging is a biomarker included as a suggestive diagnostic feature in the consensus diagnostic criteria for DLB. 123I-FP-CIT SPECT is the most widely used form of such dopaminergic imaging. Studies using FP-CIT and consensus clinical diagnosis as the standard report good sensitivity of 78% and specificity of 90% for differentiating AD from DLB. However, there has been little autopsy assessment of its validity. Two small previous studies reported aspects of the pathology of DLB cases with FP-CIT neuroimaging. We conducted an autopsy validation study of FP CIT imaging for the clinical diagnosis of DLB utilising tissue from 55 subjects in the Newcastle Brain Tissue Resource (NBTR).

Methods: We included all subjects over 60 with dementia who had donated their brain tissue to the NBTR and who had had FP CIT imaging in research studies. Included subjects came from clinical research studies in London and Newcastle. Detailed clinical research assessments and diagnoses were applied by consensus panels using international diagnostic criteria. All subjects had a baseline FP CIT scan and these were rated by blinded panels as normal or abnormal. They were reviewed in prospective studies until death and then underwent autopsy and standard neuropathological diagnoses were applied by an experienced consultant academic neuropathologist.

Results: 33 DLB and 22 AD subjects were included. Against autopsy diagnosis FP CIT had a balanced diagnostic accuracy of 86% (sensitivity 80%, specificity 92%), compared with clinical diagnosis whose accuracy was 79% (sensitivity 87%, specificity 72%). Importantly 10% of subjects with clinical DLB met pathological criteria for Lewy body disease but had had normal FP CIT imaging. Eight subjects (two false positive and six false negative cases) were misclassified by FP-CIT imaging versus gold standard neuropathology confirmed diagnoses.

Conclusion: This large autopsy series shows FP-CIT is a valid and accurate biomarker of DLB in the context of neurodegenerative dementia. The specificity in this study of FP-CIT diagnosis was 20% higher
than clinical diagnosis. However, a normal scan in DLB does not exclude Lewy body disease with little brainstem involvement, since consistent with other reports 10% of DLB subjects had normal FP-CIT scans. These important cases and other misclassified cases will be reviewed during this presentation to help elucidate our understanding of the pathology of DLB and its relationship to FP-CIT imaging.

S21.4 | Thalamic involvement in cognitive and behavioral symptoms in Dementia with Lewy Bodies (DLB): Magnetic resonance evidence
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The thalamus regulates and synchronizes distributed cortical networks supporting large-scale cerebral dynamics related to goal-directed behaviors and awareness (Schiff 2008). Particularly, phenomenal consciousness is generated by synchronized neural activity in thalamic neurons and thalamic activity is driven by information arising from the cortical computation (Ward 2011). Of note, DLB patients were clinically characterized by spontaneous alteration in cognition, attention, and arousal (Lee et al. 2012). These symptoms were reported as fluctuating cognition (flCog), which represents, together with visual hallucinations and extrapyramidal signs, the core clinical features of DLB (McKeith et al. 2005). Interestingly, the cholinergic system is more affected in DLB patients than in Alzheimer’s disease (AD) patients (Kotagalet al. 2012). This concept is amply supported by pharmacological evidences which suggest that (1) anticholinergic drugs can induce a symptom profile of altered arousal comparable to flCog in DLB (Perry et al. 1999) and (2) cholinesterase inhibitors can significantly improve flCog in DLB (Onofrj et al. 2003; Wesnes et al. 2005). We hypothesized that cholinergic imbalance within thalami and damage of the structural connectivity between thalami and cortical regions regulating alertness and attention are associated with flCog in DLB. Multimodal techniques, including structural magnetic resonance imaging (MRI), diffusion tensor imaging (DTI) and proton MR Spectroscopy (1H-MRS) was used to assess thalamic connectivity and neurochemistry in a cohort of 16 DLB, 16 AD and 13 healthy subjects. The combination of structural MRI and DTI allows parcellation of the thalami according to their cortical structural connectivity and to evaluate microstructural integrity in each connectivity-defined region. 1H-MRS technique assesses, in-vivo, different metabolites such as N-acetyl-aspartate (NAA) and total choline (tCho) which are specifically related to decrease of neuronal integrity and to cholinergic deficits respectively. The comparison between DLB and AD was performed to assess whether any possible structural and metabolic changes in the thalami were specific of a dementia characterized by the presence of flCog (DLB) or more as a result of a process of dementia per se. Furthermore, the variation of severity and frequency of flCog among DLB patients provides a means by which to assess whether the thalamic alteration are associated with more overt flCog. As compared with controls, DLB patients showed bilateral micro-structural alteration within thalamic regions projecting to prefrontal and parieto-occipital cortices, whereas AD patients showed bilateral micro-structural damage within thalamic region projecting to temporal cortex. Compared with controls, the NAA/total creatine (tCr) and higher total tCho/tCr values were lower in DLB patients. tCho/tCr were higher in the right thalamus of DLB patients as compared with AD and controls. In DLB, the tCho/tCr increase correlated with severity and frequency of flCog and the damage of thalamic regions projecting to parieto-occipital cortex were related to NPI hallucination item scores. Based on the central role of thalamic neurons in regulating arousal and visuo-spatial attention, we posit that the alteration of parieto-occipito-thalamic connectivity and the cholinergic imbalance within thalami could be central to the etiology of core symptoms characterizing DLB patients.

References:


**SYMPOSIUM 22**

The base of evidence in controversial issues

**S22.1 | Clozapine in refractory schizophrenia: Review of the evidence**

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**Introduction:** Clozapine is efficacious in up to one-third of treatment-resistant patients with schizophrenia and it remains the only medication with regulatory approval for patients with treatment-refractory schizophrenia. In addition, it may possess significant effectiveness for patients with treatment-resistant bipolar disorder. Long-term treatment with clozapine is associated with overall reduction of risk of suicidal behaviours. Moreover, it can reduce violence and persistent aggression in patients with schizophrenia and other psychiatric disorders and has been found to reduce relapse and re-hospitalization rates, whilst it takes longer to discontinuation compared to other first generation antipsychotics.

**Methods:** All randomized evidence from the available antipsychotics used for treatment-resistant schizophrenia was recently integrated using the network meta-analysis (NMA) method, excluding, however, at least three large unblinded studies [1]. Furthermore, NMA was used to investigate the effect of second-generation antipsychotics on cognition in patients with schizophrenia [2].

**Results:** Blinded randomized evidence challenges the superiority of clozapine compared to other second-generation antipsychotics against several years of clinical experience and observational evidence. Moreover, clozapine had positive effects only on verbal fluency similar to olanzapine.

**Conclusions:** RCTs included in the NMAs measure psychopathology change which may not be the optimal outcome to measure following treatment with antipsychotics; being no longer self-injurious, no longer hospitalized in the long-term, or no longer assaulting people may present more realistic outcomes in patients’ remission, adherence and functioning. In clinical practice, clozapine is largely underused...
across the world, possibly owing to the fear of its adverse effects. Results from NMA studies risk further discouraging its prescription to the seriously-ill patients that are typically not included in randomized control trials. Furthermore, NMA results could indicate a problem of the individual randomized control trial included in the NMA rather than of clozapine.

References:

S22.3 | Charting the knowledge of bipolar therapeutics
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Until recently the treatment of bipolar disorder was considered to be straightforward and was based on the use of the so-called mood-stabilizers. However this was the academic approach which had not been adopted by most clinicians around the world, as pharmacoepidemiological data suggest. Recent systematic reviews on the issue suggest that the confidence in the way we used to treat bipolar disorder is not sufficiently supported by the data; on the contrary at least in some areas different treatment approaches seem to be appropriate in contrast to the widespread and usually recommended. The biggest problem is the fragmentation of bipolar disorder in three isolated phases in research papers and the lack of data concerning most clinical aspects and issues. The design of the studies is inadequate, reporting of the results is poor and incomplete and research designs make little sense for a variety of reasons.

SYMPOSIUM 23

Ears, eyes and mind: The “SENSE-Cog Project” to improve mental well-being for elderly Europeans with sensory impairment

S23.2 | Cognitive assessment of adults with hearing and/or vision impairment
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Introduction: It has been reported that 51.4% and 26.4% of people with dementia (aged 60 to 89 years old) living in care homes had visual impairment using the visual acuity <6/12 and visual acuity <6/18 cut-offs respectively (Bowen et al., 2016). Hearing impairment defined by pure-tone thresholds has been also found in up to 90% of those who have dementia in care homes (Gold, Lightfoot, & Hnath-Chisolm, 1996). Most commonly used cognitive tests include items that must be seen or heard (Dupuis et al., 2015). Sensory impairment may therefore confound cognitive testing or preclude adequate cognitive evaluation. A scoping literature review has been carried out to identify cognitive assessments that have been adapted for use with adults with hearing and/or vision impairment and to report on i) how they have been adapted, ii) attempts to validate the adapted version of the test, and iii) evaluate cultural neutrality and availability in EU languages.
Method: Electronic databases were searched using key terms “hearing disorders” or “vision disorders” and “cognitive assessment”. Database searches were supplemented by searching through the reference lists of papers that met the inclusion criterion for the review and via consultation with a network of health professionals to identify additional literature not identified via the database search.

Results: 2056 papers were identified and out of these papers only 20 papers fitted for inclusion. 4 cognitive tests adapted for hearing impairment and 16 cognitive tests adapted for vision impairment were identified. 11 papers reported adaptations of the MoCA and MMSE for hearing and vision impaired individuals. Adaptations for patients with hearing impairment involved deleting hearing-dependent items or changing the tests to written versions, by presenting test items in flashcards or on a computer screen. Adaptations for patients with vision impairment involved deleting vision-dependent item or spoken versions of vision dependent tasks (e.g. verbal clock draw task).

The few studies that reported validation of the modified versions of the tests revealed that item deletion had a negative impact on sensitivity and specificity, particularly in relation to detection of mild cognitive impairment. The MoCA and MMSE are available in 23 out of the 24 official EU languages (apart from Maltese), whereas most of the other tests are only available in English.

Discussion: Some attempts have been made to devise or adapt cognitive tests for people with hearing and/or vision impairment. The primary limitations of these adaptations are that: i) the validity of the adapted scales has not been established. It is likely that sensitivity and specificity of the adapted versions are poorer than the original test, especially if adaptation involved item deletion; ii) many adapted tests are not readily available in languages other than English. One possible solution is to substitute sensory-neutral items to replace deleted modality-specific items, and re-validate the adapted versions of the tests with new normative samples. Adapted tests will also require translation into the main European languages.

S23.3 | Interventions to support hearing and vision in patients with dementia
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Background: The aging society in the EU is increasingly confronted with different challenges, as to the changes of the physical and psychological functioning of the human being. There is an enormous finding in cognitive sciences, which focus on the prevalence of mental disorders and other disorders of the brain in Europe (e.g. Wittchen et al. 2011). Apart from that, there are also ongoing pathological changes in sensory functioning. Hereby epidemiology studies show that there is an increase in hearing and vision impairment in the aging population (Lin et al. 2011, Evans et al. 2002). This increase can be accompanied by neurocognitive disorders. Yet there are findings that focus on interventions regarding hearing or vision loss and improving cognition or mental well-being, but there is just little evidence on results facing the triple challenge (hearing/vision/cognition). However, how can we contribute to improve cognition or quality of life through a non-invasive intervention in elderly people with hearing, vision and cognitive problems (here: dementia)?

Objectives: Therefore the aim of this systematic review is to assess the impact of treating hearing and vision impairment on i) cognition, ii) rate of decline, iii) psychiatric symptoms, iv) hearing/vision-related quality of life, v) general quality of life and vi) caregiver burden for adults with dementing conditions. Studies were included regarding the inclusion criteria: age 60+, dementia, hearing impairment, vision impairment. Likewise, the focus of the review is on treatment, involving invasive and non-invasive procedures (e.g. surgical interventions, behavioural interventions, problem-solving-training etc.).
Search Methods: We searched different electronic databases (CENTRAL, MEDLINE, EMBASE etc.) systematically by using key terms and their synonyms: dementia, hearing impairment, vision impairment, intervention and management. Clinical trials, nonrandomised studies, case-control and cohort studies were included. The database searches were supplemented by searching through bibliographies of papers that match the eligibility criteria and via consultation with a network of health professional experts to identify additional grey literature that has not been found via the database search.

Selection criteria: Focus here is primarily on interventions regarding improving cognition in elderly with dementia having hearing and vision problems.

Data collection and analysis: Two independent reviewers did Screening of both titles and abstracts. All disagreements were resolved by discussion or consultation with a third reviewer if necessary. The whole process underwent the PRISM procedure. Risk of bias assessment and data analysis will be completed and reported in a narrative review using Newcastle Ottawa Scale and Cochrane methods.

Discussion: There is a bunch of studies concerning interventions (invasive/non-invasive) in hearing and vision impairment, which reveal positive outcomes for older adults with dementia. In hearing, the focus of the most studies is mainly on speech and hearing aid intervention to improve mental well-being, whilst in vision there are several studies, which target mainly on psychosocial outcomes. Most of them do not include people with dementia. Another problem is that studies, realised as an RCT, have small sample sizes, so that is not sure if they are meaningful.

References:

SYMPOSIUM 25
New advances in FTLD

S25.1 | The genetic and molecular basis of frontotemporal dementia

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Frontotemporal dementia (FTD) is the second commonest cause of presenile dementia, often affecting individuals below 65 years. It is characterized clinically by behavioral changes, executive dysfunction and/or language impairment and pathologically by frontotemporal lobar degeneration (FTLD). It is commonly associated with atypical parkinsonism and/or amyotrophic lateral sclerosis (ALS). In fact, FTD and ALS are now considered opposite ends of a disease spectrum based on clinical, pathological and genetic data.
From a clinical perspective, FTD is subdivided into behavioral variant FTD and primary progressive aphasia (PPA). PPA is further subdivided into semantic variant and non-fluent variant. A logopenic variant PPA is also increasingly recognized. The FTD spectrum further encompasses patients with corticobasal syndrome, progressive supranuclear palsy and, importantly, FTD-ALS, more commonly seen in behavioral variant FTD, but also present in PPA. The clinical heterogeneity of FTD reflects the pathological heterogeneity of FTLD, which is further linked to the numerous genetic causes underlying the disorder.

Important recent advances in the neuropathology of FTLD have allowed a comprehensive overview of its heterogeneous molecular basis. Originally, FTLD was classified into FTLD-tau, characterized by the presence of tau-positive inclusions, and FTLD-U, characterized by the presence of ubiquitin-positive inclusions. Since 2006, TDP-43 has been recognized as the protein that accumulates in the majority of ubiquitin-positive cases. TDP-43 also accumulates in the majority of ALS cases, thus linking FTD and ALS at a molecular level. A minority of FTLD-U cases, which are TDP-43 negative, stain positively for the FET protein family.

Up to 40% of patients with FTD have a positive family history and around half of these display clear autosomal dominant inheritance. Important recent advances in the genetics of FTD have allowed the identification of genes responsible for the majority of autosomal dominant cases. These genes also underlie a small but significant percentage of apparently sporadic FTD. Genetic advances combined with advances in neuropathology have uncovered the complex molecular picture of familial FTD. Mutations in MAPT, underlying FTLD-tau, and mutations in GRN and C9ORF72, underlying the majority of FLTD-TDP, are the three common genetic causes of FTD. Importantly, a non-coding hexanucleotide repeat expansion in C9ORF72 has emerged as the commonest genetic cause of FTD-ALS and pure ALS. FTLD-TDP can also be caused by much rarer genes, such as VCP (also causes inclusion body myositis and Paget’s disease); TARDBP (usually associated with ALS); SQSTM1 and TBK1. Although the neuropathology of sporadic FTD is analogous to the familial form, far less is known regarding the influence of disease modifier genes on sporadic disease. Limited GWAS data have recognized TMEM106B and more recently the HLA-locus and RAB38 locus as possible risk factors.

Emerging neuropathological and genetic data have allowed the delineation of specific molecular pathways that are likely implicated in FTD. Both loss- and gain-of-function mutations can underlie the accumulation of different protein inclusions, which may trigger neurodegeneration. Prion-like propagation of protein aggregates is being currently investigated as a possible mechanism of disease spreading and progression in FTD.

S25.3 | Pointing towards a specific protein
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Frontotemporal Lobar Degenerations constitute a heterogeneous group of disorders with different pathologies and biochemical mechanisms involved, the most common being tauopathy and TDP-43 proteinopathy. Common clinical presentations include frontal and behavioral symptoms accompanied by a frontosubcortical type of cognitive decline. However, there are some clinical signs and symptoms which may point to a certain degree towards a specific proteinopathy. The presence of motor-neuron signs points toward TDP-43, although it may also occur in FUS-proteinopathy. Significant psychosis (sometimes reminiscent of Lewy bodies) also points towards TDP-43. The presence of parkinsonism and especially features of progressive supranuclear and/or corticobasal syndromes are almost always associated with tauopathy. Language disorder consistent with the non-fluent agrammatic type is associated with tauopathy.
in ¾ of patients. However, semantic aphasia is associated mainly with TDP-43 proteinopathy in ¾ of patients. The presence of myopathy and/or Paget’s disease points towards mutations of the VCP gene. The combination of corticobasal syndrome with primary lateral sclerosis-like syndrome may be observed in FUS. A very early onset of behavioral syndrome with hyperphagia, hypersexuality and obsessive-compulsive features and with striatal atrophy is observed in FUS. The above symptoms are not pathognomonic, but may be of significant help. The use of CSF biomarkers may further assist in the identification of the specific proteinopathy underlying the clinical presentation.

SYMPOSIUM 26
From genes to domains of functioning: Endophenotypes in bipolar disorder

S26.1 | The emerging molecular genetic architecture of bipolar disorder
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Although clinical genetic studies (family, adoption and twin studies) during the last decades have confirmed that Bipolar Disorder (BD) is familial and one of the most heritable adult-onset major psychiatric disorders, molecular genetic research in this debilitating disease has entered an era of maturity only during the last 5 years. Genome-wide association studies (GWAS) have produced for the first time replicated associations with distinct genetic loci, such as ANK3 and CACNA1C, yet explaining only a small percentage of the heritability of BD previously reported in twin studies. Novel molecular genetic tools (polygenic scores, SNP-heritability) have recently captured part of the previously “missing heritability”. Follow-up studies of findings from molecular genetic studies investigate their functional significance while pathway analyses have highlighted the role of the calcium channel signaling pathway. As clinical and genetic heterogeneity of BD has been considered as mainly responsible for the slow progress so far, deconstructing the phenotype seems highly promising. Endophenotypes, which lie in between genes and diagnostic categories, have recently been the focus of extensive research. Several candidate endophenotypes have been proposed, including those related to neurocognitive functioning as well as those related to circadian activity and sleep patterns, which will be discussed in the symposium in more detail.

S26.2 | Cognitive endophenotypes in bipolar disorder: Weighing the evidence
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Bipolar disorder (BD) is a highly heritable condition, as demonstrated by clinical genetic studies. However, progress in identifying its genetic basis has been slow, probably due to genetic complexity and phenotypic heterogeneity. The identification of endophenotypes, that are quantifiable traits reflecting more proximal effects of genes, has been proposed as an alternative strategy. Growing evidence illustrates that patients with BD show cognitive deficits both during the acute phase of illness and during remission. Several neurocognitive functions have been proposed as potential endophenotypes of BD. Evidence from studies
in euthymic BD patients, first manic episode patients, family and twin studies are reviewed in this presentation in relation to the endophenotype concept and criteria. Despite methodological limitations and inconsistency across studies, impairment in declarative memory (verbal, facial), and executive functions (working memory, set shifting and interference) seem to be the most prevalent candidates. The lack of disease specificity, the interrelationship between cognitive functions as well as misgivings regarding their genetic simplicity has caused debate over the utility of neurocognitive endophenotypes in BD. However, the fact that they are easily quantifiable traits makes them suitable for large sample genetic analyses.

S26.3 | Circadian activity and sleep-related endophenotypes in bipolar disorder
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Sleep disorder is a quite prominent symptom both in depressive as well as manic episodes of bipolar disorder. In addition, residual insomnia during euthymic periods is associated with an increased risk of affective relapse and/or with inadequate recovery from the previous episode. Moreover, there are certain particular characteristics of insomnia which are shown to be most consistently impaired in euthymic bipolar patients. It thus seems that there exists a bidirectional relationship between affect regulation and particular sleep mechanisms, while various lines of evidence suggest that circadian rhythmicity anomalies may have casual effects on the development of bipolar episodes. Finally, there seems to be a relationship between sleep disorders and other types of symptomatology of affective disorder including the degree of cognitive impairment and suicidality. Various sleep-related genes, mainly those pertaining to circadian rhythms, have been found to be associated with the probability of developing bipolar disorder or with certain of its clinical characteristics, but the results are still inconclusive. Given the above, there is emerging evidence that circadian activity and other sleep-related characteristics may constitute endophenotypes for bipolar disorder, although no particular characteristic meets yet all criteria for being formally considered as proper endophenotype for the disease.
Case Reports

CR1 | Antiepileptic-induced psychosis is a possible predictor for post temporal lobectomy alternate psychosis

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Introduction: Temporal lobectomy is a treatment modality for resistant epilepsies. Alternate psychosis is one of the many post surgical adverse events of a temporal lobectomy. Alternate psychosis describes the clinical phenomenon of the reciprocal relationship between seizures and psychosis, without relying on electroencephalogram (EEG) findings[1]. Examples of predictors of post lobectomy psychosis include pre surgical presence of psychiatric diseases, laterality of seizure focus and age at time of surgery[2]. A case of topiramate induced psychosis leading to post temporal lobectomy alternate psychosis is presented.

Clinical Description: A 36-year-old female suffered from epilepsy since childhood. She had seizures at the rate of 2-3 times per day. Her seizures started with blank staring and oral automatisms, with left upper limb dystonia and right head deviation. This was accompanied by drooling of saliva, up rolling of eyeballs and postictal drowsiness for approximately 30 minutes. Whilst on topiramate, the patient started experiencing auditory and visual hallucinations. She also had persecutory delusions whereby she believed her sister was trying to harm her and delusions of jealousy whereby she believed her husband was having an affair. While on topiramate, her seizures continued. The medication was subsequently stopped and her psychosis resolved. Magnetic Resonance Imaging (MRI) of the brain in 2002 showed right mesial temporal sclerosis. Video-EEG telemetry showed right anterior temporal interictal discharges and nine focal seizures with right temporal ictal onset in seven seizures. A right temporal lobectomy was planned. Post-surgery she became seizure free. Two weeks after her surgery, a re-challenge was done with topiramate, but she did not have any psychosis thereafter. One month later however, she developed a delusional jealousy, believing that he was having an affair. Two days later, she started experiencing auditory hallucinations, hearing a voice asking her to die and commenting that she was useless. She experienced thought broadcasting, believing that others could read her mind. She was initiated on 15mg ON of olanzapine and her psychosis resolved completely after one month. Throughout her psychosis post surgery, she was seizure free.

Discussion: Psychosis post temporal lobectomy can be attributed to either de novo psychosis or alternate psychosis. De novo psychosis is unlikely in this case, as the psychosis was well formed and prolonged. Theories explaining this phenomenon of alternate psychosis states that epileptiform discharges may mimic electroconvulsive therapy in a focal area and this seizure abatement may lead to psychosis. Long term potentiation and kindling phenomenon have also been proposed[3].

Conclusion: Precautions should be taken when antiepileptic drug-induced psychosis occurs, as this could serve as a predictor for post lobectomy alternate psychosis.

References:
3 Ntsanwisi VTR, Rataemane ST, Magazi DS. Alternative psychosis (forced normalisation) in epilepsy. South african journal of psychiatry 2011;17.
Familial frontotemporal dementia with myopathy due to Valosin Containing Protein (VCP) mutation

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Background: Mutations in the Valosin Containing Protein (VCP) gene have been recently identified as a rare cause of familial frontotemporal dementia (FTD), amyotrophic lateral sclerosis (ALS), inclusion body myopathy and Paget’s disease of bone. Here we present the first Greek case of familial myopathy FTD-ALS syndrome in which a VCP mutation was identified.

Clinical Description: A 62 year-old male patient presented with a slowly deteriorating gait difficulty starting 15 years ago, which aggravated seriously during the last year. Alongside this last year he manifested neuropsychiatric symptoms like aggression, apathy, palilalia and obsessions. The neurological examination revealed diffuse muscle atrophy involving both upper and lower extremities. In the neuropsychological evaluation conceptualization, mental flexibility and motor programming were affected. Brain MRI revealed frontal and temporal atrophy and few white matter lesions, while the electromyography confirmed muscle fiber loss and spontaneous activity. Muscle MRI showed diffuse muscle atrophy. Skeletal radiographs did not reveal any signs of Paget’s disease. According to family history, his mother passed away at the age of 63 after developing dementia-like symptoms. One of his three brothers was diagnosed with ALS and died at the age of 53, while another brother presented with behavioral symptoms from the age 60.

A diagnostic genetic test was conducted that confirmed the clinical suspicion of a heterozygous missense mutation p.R159H (c.476G>A) in the VCP gene.

Discussion: Inclusion body Myopathy, Paget’s disease of bone, Frontotemporal dementia and/or Amyotrophic Lateral Sclerosis (IBMPFD) can be caused by a single heterozygous mutation in the VCP gene. The syndrome can be partially or fully developed depending on the respective mutation. Although the exact pathogenic mechanism by which VCP mutations cause neurodegeneration remains unknown, dysregulation of autophagy, through ubiquitin and TDP-43 pathology has been demonstrated.

A case of probable multiple system atrophy with prominent behavioral symptoms

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Introduction: Multiple system atrophy (MSA) is a rare neurodegenerative disorder that manifests with dysautonomia, cerebellar ataxia, parkinsonism and pyramidal signs, with relative preservation of cognitive function. Prominent neuropsychiatric symptoms are extremely rare in this condition.

Clinical Description: This 66 year old male presented with a 5 year history of REM sleep behavior disorder (RBD). Over the past 3 years he developed a progressively deteriorating ataxia, followed by bradykinesia and dysautonomia. At the same time, he exhibited neuropsychiatric symptoms, mainly irritability, aggression, apathy, disinhibition and aberrant motor behavior. Furthermore he manifested compulsive – ritualistic behavior (including hoarding) as well as hyperorality and dietary changes. He had a mild frontal – dysexecutive syndrome at formal neuropsychological testing. His DaT-scan was abnormal, as expected in MSA. His brain MRI was typical of MSA-C, as it exhibited the “hot-cross bun” sign, hypertense and atrophic middle cerebellar penducles,
alongside cerebellar atrophy. He had a slightly asymmetrical (right > left) parietal, temporal and frontal atrophy and few, mostly frontal, subcortical white matter lesions. The atrophy included the medial frontal lobe, the anterior operculum, the insula and the frontal poles, regions important for behavior regulation.

Discussion: Our patient fulfills the diagnostic criteria for both MSA-C and bv-FTD. As neuropsychiatric symptoms are extremely rare in MSA, the possibility of random co-existence of both disorders cannot be excluded. However, the simultaneous presentation of two rather rare diseases in the same patient is intriguing, since it could imply possible interactions among more than one cardinal proteinopathy (α-synucleinopathy, tauopathy and/or TDP43 proteinopathy).

Conclusion: Patients with MSA may rarely exhibit severe neuropsychiatric symptoms reminiscent of bv-FTD.

CR4 | White matter abnormalities in a woman with anorexia nervosa: A case report and review of the literature
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Background: Anorexia nervosa is a life threatening disorder, without established pathophysiological evidence. Neuroimaging plays an important role in identifying brain abnormalities in psychiatric disorders. There are few studies reporting gray and white matter alterations in anorectic patients, with MRI playing a major role in the identification of such abnormalities using advanced MR techniques.

Case Presentation: In our case report we present the clinical and imaging findings of a young patient with anorexia nervosa. The patient had white matter abnormalities located at the posterior limb of the internal capsule bilaterally. Using Diffusion Tensor Imaging microstructural changes were also identified at the anterior part of the cingulum.

Conclusion: White matter abnormalities may be present in anorexia nervosa. It seems that the limbic system and its connections to other parts of the brain play important role in the pathophysiology of anorexia nervosa.

CR5 | Severe psychogenic pruritus in an elderly woman: A case report
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Introduction: Chronic pruritus (lasting >6 weeks) represents the most common skin condition in people over 65 years old. When other causes have been ruled out -dry skin, sub-clinical eczema, various types of cancers, kidney and thyroid abnormalities, ferrum insufficiency etc- it is considered as “psychogenic”.

Clinical Description: 88 year-old woman suffering from moderate to severe dementia arrives at the psychiatric emergency department accompanied by her younger sister –being also her caregiver. She complains of, almost unstoppable, pruritus. The symptom lasts for nearly 1½ year and is mainly focused in the areas of the forehead, the scalp, and around the eyes (the patient had even mildly injured her eyelids). All possible causes of chronic pruritus had been ruled out; the patient had been subjected to complete blood tests whilst repeated dermatological consultations had been fruitless. She was under rivastigmine 12mg/day, memantine 10mg/day, escitalopram 10mg/day, mirtazapine 15mg/day, alprazolam 0.5mg/day. The patient also suffered from hypertension and (mild) Parkinson’s disease which were both under treatment. She had been given two antihistamines in succession: desloratadine 5mg/day and
levocetirizine 5mg/day without any significant improvement. We considered that a focused change in her medications should be made, while, concurrently, her treatment schema needed to be simplified (always an important goal in the elderly). First step: discontinuation of levocetirizine, gradual elimination of alprazolam and adjunct of quetiapine 50mg/day. Antihistamines may deteriorate memory function in the elderly -when ineffective, they should be stopped. Quetiapine was added aiming to gradually withdraw alprazolam—a medication related to confusion in the elderly- whilst dealing effectively with anxiety and sleep problems. Two weeks later the patient’s clinical status was unaltered -but with fewer medications. Second step: a focused literature search on PubMed led into prescribing gabapentin 600mg/day—which gradually reached 900mg/day- for the pruritus. Concurrently, mirtazapine was discontinued. After three weeks considerable improvement was noticed regarding the intensity and the duration of the pruritus. Third step: given that the dementia was moderate to severe, we increased memantine to 20mg/day, discontinued rivastigmine, and increased escitalopram to 20mg/day. The latter was decided in order to fully exploit the potential synergy between the antidepressant (escitalopram) and gabapentin—both recommended in cases of psychogenic pruritus. Assessments after 1 and 3 months: further improvement in pruritus’ intensity, duration and extent—now limited in the area around the eyes-, and better mood.

Discussion: Psychogenic pruritus mainly afflicts elderly individuals over 85 years old, predominately females; it is usually centered in the face and scalp areas. Itch is thought to be mediated by the central nervous system’s opioid neurotransmitters, hence the similarities between the senses of itch and pain. Depression has also been related to the intensity and frequency of psychogenic pruritus. It follows that medications involved in the treatment of pain and/or depression—e.g. gabapentin, pregabalin, SSRIs, SNRIs—are suggested for psychogenic pruritus as well.

Conclusion: Psychogenic pruritus’ impact on the patients’ quality of life can be devastating. It also represents a therapeutic challenge because it frequently afflicts elderly patients with several comorbidities and complex pharmaceutical schemas.

References:

Statement: The authors declare that they have no conflict of interest.
Depression and dementia are both common conditions in old age, and frequently occur together. The inter-relationship between the two clinical entities is complex and still not well understood and further work is needed on examining the temporal relationship and underlying neurobiological networks in order to draw more confident conclusions as to whether the two conditions are linked as risk factors, are part of a continuum, or are two separate conditions. Data from the existing literature devoted to the relationships between dementia and depression can be controversial on account of methodological biases such as differing definitions, variability of assessment tools for both depression and dementia, length of follow up, as well as the primary aim of the study. Themes emerging from existing studies regarding the relationship have generated a number of different hypotheses. These include (1) depression being an independent risk factor in developing dementia; (2) depression affecting the threshold for manifesting dementia; (3) dementia or cognitive impairment being a feature of depression; (4) the notion of depression being a prodrome of dementia; (5) depression being a reaction to cognitive decline and finally, (6) dementia and depression sharing common risk factors explaining the increased prevalence of both in this population, and why they are frequently comorbid.

Objectives: To review literature supporting depression being a risk factor, a prodrome, a consequence, or an independent comorbidity in dementia.

Results: Growing evidence is now showing that the association is complex with epidemiological studies suggesting depression to be an independent risk factor for dementia but importantly the timing of depression is significant. In particular, earlier life depression has been associated with a more than twofold increase in dementia risk. By contrast, studies of late-life depression and dementia risk have been conflicting, with some studies suggesting that depression occurring in later life is a prodrome to dementia as opposed to a risk factor. Establishing the temporality of the relationship has been highlighted as being important. However, with the prodromal pathology phase of dementia extending 10 years or more before clinical diagnosis, it is not always straightforward to determine which symptoms occurring years before the onset of dementia were intrinsic to its development and which were independent. Overall there is convincing evidence to support both the notion that early life depression can act as a risk factor for later life dementia, and that later life depression can be seen as a prodrome to dementia. There is also evidence to support both conditions showing similar neurobiological changes, particularly white matter disease, either indicating shared risk factors or a shared pattern of neuronal damage.

Discussion: When looking at the causative/risk factor hypothesis it will be interesting to find out whether future research looking at the treatment of mood disorders shows any reduction in risk of dementia. The prodromal hypothesis highlights the need to carefully follow up individuals presenting with depression in old age for future cognitive decline, especially when the first depressive episode occurs in later life. Additionally, research drawing more confident conclusions about the underlying neurobiological pathways, may pave the way for more effective treatment of both depression and dementia.
FC2 | IDEA: Intervention to prevent Depressive symptoms and promote well-being in EAry stage dementia: Development and feasibility

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Introduction: People with dementia are at risk of depressive symptoms, and loss of enjoyment of life. Medications such as antidepressants are ineffective and have significant side effects. We therefore must find other ways to prevent and treat depressive symptoms in people with dementia. A systematic review of psychological interventions for people with dementia has shown potential of effectiveness of ‘talking therapies’ for depressive symptoms. However, most studies tested feasibility rather than clinical effectiveness.

Methods: This talk will describe the IDEA study, funded by the Alzheimer’s Society, which will develop and test the feasibility of an intervention based on activity scheduling of pleasant events to prevent depressive symptoms in people with early-stage dementia.

Results: In the second part of this talk we present preliminary results of a meta-analysis of a systematic review of the clinical effectiveness of behavioral activation interventions for depression in older people including those with cognitive impairment.

Conclusion: The combination of these disorders places an enormous emotional burden to people living with dementia and their families, which may result in even greater direct health care costs compared to each condition alone. Given limited treatment options available offering interventions that prevent depressive symptoms is even more critical and timely.

Source of Funding: This study is funded by the Alzheimer’s Society.

FC3 | Predictors of depression with onset in later middle-age

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Introduction: Depression is associated with significant morbidity and disability. The incidence of major depression peaks in the 20’s, but it is not uncommon for individuals to experience onset later in life. The Vietnam Era Twin Study of Aging (VETSA) presents an opportunity to investigate putative risk factors for depression with onset in later middle-age using prospective data obtained prior to onset.

Methods: Data were collected from approximately 1,200 participants in VETSA. The sample comprises men who served in the military between 1965 and 1975. The demographic characteristics of VETSA participants is very similar to that of 2003 U.S. Census data for men in their 50s in education, median self-income, ethnicity, marital status, and employment. VETSA includes data that were collected at the time participants entered the military (average age 20), as well as data collected in the Harvard Study of Drug Abuse when the average age of participants was 41 years. During the first and second waves of VETSA data collection subjects were 55 and 62 years old on average, respectively. As part of the second wave of VETSA, participants completed the Center for Epidemiologic Studies Depression Scale (CESD) which has excellent reliability and is considered a valid indicator of clinically meaningful depression. In the Harvard Study of Drug Abuse participants completed the DIS-III-R diagnostic interview. In the present study we excluded subjects with an onset of depression before the age of 42.
Results: During the second wave of VETSA, 14.4% of participants had current depression based on the CESD. Participants were asked how old they were the first time they had depression. Among those with an onset of depression after age 41 years who are the subject of this report, the mean age of onset was 53.7 years (SD=5.2; range = 42.0 to 64.0). Among all participants with current depression, 74.5% had onset after the age of 41 years. We examined the presence of psychopathology before age 42. The odds ratio (OR) relating depression to a DSM-III-R diagnosis of dependence on any illicit drug was 2.1. The OR for DSM-III-R nicotine dependence was 1.7 and for alcohol dependence the OR was 1.9. Participants with current depression had lower cognitive ability and significantly fewer years of education (11.9 versus 12.4) at age 20 when they were inducted into the military. In terms of ‘normal’ personality, participants who were depressed at age 62 had significantly lower Positive Emotionality and significantly higher Negative Emotionality at age 55.

Conclusion: A substantial proportion of the subjects who were depressed at age 62 had experienced onset after age 41. Several common types of substance dependence (illicit drugs, nicotine, and alcohol) occurring before the age of 42 are risk factors for the development of depression after age 41, approximately doubling the odds of depression. Poorer cognitive ability and lower education at age 20 are also risk factors for late onset depression.

FC4 | Perceived depression and depressive symptoms among NCDs patients attending primary health centers in Dubai UAE 2014

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Background: Depression is an important public-health problem and one of the leading causes of disease burden worldwide. Depression is often comorbid with other chronic diseases and can worsen their associated health outcomes. Few studies have explored the effect of depression, alone or as a comorbidity, on overall health status.

Objectives: To study the prevalence of depression and depressive symptoms among NCD patients attending PHC at Dubai Health authority facilities, Dubai, UAE. To study the distribution of socio-demographic determinants of the NCD patient presented with depression or depressive symptoms. To study some associated risk factors

Methodology: A cross-sectional study has been carried out among randomly selected sample of 306, both males and females (patients with different chronic diseases status attending primary health care facilities at Dubai health authority in Dubai for the year 2014. Sample size estimated using Epi–info software and was 306. Sample type was multistage stratified random sample with proportional allocations from different primary health care centers both in Diera and Bur Dubai sides. Interview administered questionnaire has been used for data collection (Depression Anxiety Stress Scales “DASS 21”). Data was analyzed using SPSS 21.

Results: The figures reflected that female proportion was 72.5%, and 73.2% of the total study population were UAE nationals. Regarding marital status, 49.3 of the study population was Married, 42.5 single, 2.3 Widowed and 2.6 divorced. 18 % of the study population presented with mild depressive symptoms as detected by DASS, 15.4% of the study population have moderate depressive symptoms and 6.5% severe depressive symptoms and extremely severe depressive symptoms were among 7.2%. The total depressive symptoms among patients with chronic diseases attending PHC clinics was 48.2%. The study reflected that age factor has no significant association with depression among chronic diseases patients.
attending primary health care centers in Dubai, UAE, P Value =0.498, the (odds ratio 95% CI of the effect of sex factor on developing of depression among NCD patients attending PHC clinic in Dubai was 1.3270(0.785-2.243). The (odds ratio 95% CI of the effect of nationality factor on developing of depression among NCD patients attending PHC clinic in Dubai was 0.641(0.369-1.114). The effect of marital status factor on developing depression among NCD patients attending PHC clinic in Dubai was not statistically significant P value =0.42.

Conclusions: Frequency rates of depression associated with chronic diseases are significantly high which reflected two direction effect, some socio-demographic factors were shown to be playing significant role such as gender and nationality. Depression intervention program at patient with NCD needs to be developed to prevent two direction negative impacts and improve quality of life and over all life expectancy.

FC5 | The microbiome – The missing link in the pathogenesis of schizophrenia
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Introduction: Recent studies indicate that individuals with schizophrenia have evidence of immune activation that may contribute to disease pathogenesis. The source of this immune activation has not been identified but is likely to be related to both genetic and environmental components.

Methods: Non systematic review of literature.

Results: Recently it has become apparent that the composition of microbes on mucosal surfaces, termed the microbiome, represents an important modulator of the immune response in humans and in experimental animals. The microbiome has been linked to the generation of an aberrant immune response and also been shown to modulate brain development and behavior in animal model systems.

Conclusion / Discussion: Research on the role of the human intestinal microbiota in the genesis and/or maintenance of psychiatric disorders is in its infancy but appears as one of the most promising avenues of research in psychiatry.

FC6 | Orbitofrontal cortex (OFC) response underlies attentional bias towards alcohol-related sounds in abstinent alcoholics
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Background: In alcoholism, alcohol-related stimuli gain salience, involuntarily capturing attention.

Methods: To test the neural basis of alcohol salience modulation of auditory attentional control, 17 sober alcoholics (ALC) and 16 controls (CTL) underwent a forced-choice dichotic listening fMRI task in which an alcohol-related sound was paired with a non-alcohol-related sound, and non-alcohol sounds pairs were baseline. Participants reported whether the attended ear sound was alcohol-related or not. We calculated whole sample BOLD activations for: a) “Alcohol sounds presented to the attended vs. Alcohol sounds presented to the unattended ear” (congruent minus incongruent), b) “Alcohol sounds presented to the unattended vs. Alcohol sounds presented to the attended ear” (incongruent minus congruent), and c) “All alcohol sounds trials minus baseline trials”, additionally performed separately for each group.
**Results:** Both groups discriminated all trial categories above chance level. “Congruent minus incongruent” invoked mesocorticolimbic activation including the right insula, OFC, caudate, thalamus, hippocampus bilaterally and left amygdala. Incongruent minus congruent activated the left cuneus and precuneus, which may underlie higher cognitive control demands and conflict monitoring. “All alcohol sounds trials vs. baseline” invoked mesocorticolimbic activation. When analyzed separately the groups differed, ALC showed bilateral OFC activation, whereas CTL showed superior and middle frontal activation.

**Conclusion:** Expanding the literature, our novel task demonstrated that orienting attention towards auditory alcohol cues invokes mesocorticolimbic activation, reflecting the subjective evaluation of alcohol rewarding effect. The OFC activation in ALC when processing alcohol-related sounds may reflect the expected rewarding experience of drinking, underlying unfit decision-making in alcoholism.
Poster Presentations

POSTER SESSION 1
Dementia – Neurology – Old-age depression

PP01 (ICGP Junior Investigator Awardee) | Symptoms associated with mild cognitive impairment in Lewy bodies disease
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Objective: Retrospective studies have reported that symptoms such as hyposmia, constipation, dizziness, anxiety, apathy and nightmares are common in the prodromal phase of dementia with Lewy bodies (DLB). We aimed to identify if a range of symptoms were more common in Lewy body mild cognitive impairment (LB-MCI) than other types of MCI in the Newcastle LewyPro prospective cohort study.

Methods: We recruited volunteers with MCI and possible symptoms of Lewy body disease (e.g. tremor, visual hallucinations, fluctuations). After a thorough clinical assessment, subjects were characterised as LBMCI if they had at least two core or suggestive of dementia with Lewy bodies. Those with no core or suggestive features were classified as “other” MCI. A symptom questionnaire was administered to volunteers and, where possible, their carers.

Results: Compared with other MCI (n=18), those with LB-MCI (n=35) were more likely to report problem solving difficulties (40% v 11%; p=0.03), a change in handwriting (74% v 28%; p=0.001), weak voice (41% v 6%; p=0.02) and drooling (51% v 11%; p=0.004), with a trend toward greater rates of hyposmia (49% v 22%; p=0.06). They were not significantly more likely to report anxiety, constipation, dizziness, apathy or nightmares, although all these symptoms were common in LB-MCI.

Conclusions: In addition to the core and suggestive features of DLB, symptoms such as problem solving difficulties, change in handwriting, weak voice and drooling may help to identify LB-MCI. Features such as constipation, anxiety and apathy may not be specific markers of LB disease.

PP02 (ICGP Junior Investigator Awards) | Hippocampal atrophy as a predictor of cognitive symptoms in dementia with Lewy bodies
G. Elder
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Objective: Dementia with Lewy bodies (DLB) and Alzheimer’s disease (AD) can be difficult to separate diagnostically, potentially due to the co-existence of AD pathology in DLB. The level of hippocampal atrophy observed within DLB is less than that of AD, although this varies considerably and reflects the variability in concurrent AD pathology. How this influences the clinical phenotype is unclear. In this study we sought to explore how hippocampal atrophy, as a proxy of AD pathology, relates to the clinical phenotype of DLB.

Methods: DLB (n = 65), AD (n = 78) and healthy control (n = 71) participants completed 3T T1 magnetic resonance imaging, cognitive (CAMCOG, MMSE), motor and neuropsychiatric assessments. Hippocampal
volume was compared between groups and regression models were used to investigate whether hippocampal volume predicted cognitive and non-cognitive symptoms in DLB.

**Results:** DLB, AD and control participants showed significantly different hippocampal volumes, where atrophy was highest in AD ($p < .001$). In DLB, total hippocampal volume predicted total CAMCOG ($p = .001$) and MMSE scores ($p < .01$), CAMCOG memory ($p < .001$) and executive function ($p < .05$) subscores, but not motor severity, hallucinations, depression, anxiety or cognitive fluctuations ($p > .05$).

**Conclusions:** These results are in agreement with other studies indicating that hippocampal atrophy is less severe in DLB than AD. These findings indicate that hippocampal atrophy is associated with the severity of cognitive, but not non-motor symptoms in DLB, suggesting non-AD related pathology is more important for the manifestation of the latter.

**PP03 (ICGP Junior Investigator Awardee) | The separate and interactive associations of urban trauma and depression on brain structure**

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Trauma and depression have each been associated with cognitive and brain structural alterations, but their combined effect on these outcomes is unclear. We investigated the separate and interactive associations of trauma and depression on cognition and brain aging in a sample of ethnically diverse urban dwellers, and explored the impact of age on these effects. 284 adults aged 30-89 were divided into four groups based on current depression and trauma history. Cognitive domains of VERBAL learning/free recall/ recognition, VISUAL learning/free recall/recognition, and speeded attention/cognitive flexibility (SA/CF) were assessed and grey matter cortical thickness and tractography-based structural connectomics were performed on T1/SPGR and diffusion tensor imaging. Multivariable linear regressions of cortical thickness revealed an association between trauma and the left prefrontal cortex; more specifically the pars orbitals, middle frontal and orbitofrontal regions. While cortical thickness of the left PFC did not mediate the associations between trauma and cognition, select subregions revealed lower efficiency metrics in tractography-derived structural connectomic analyses of the brain. Trauma, regardless of Depression, is associated with worse verbal learning and memory performance but not recognition, particularly in older adults. When taken together with our neuroimaging findings, this suggests that the retrieval problem seen in the presence of Trauma may be related to altered PFC network efficiency. Clinicians working with older adults in urban settings should query for trauma in addition to depression when considering subjective and objective measures of cognition.

**PP04 (ICGP Junior Investigator Awardee) | Plasma levels of lipoprotein (a) and apolipoprotein A1 in patients with probable Alzheimer’s disease**

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**Introduction:** Apolipoproteins have been implicated in the pathogenesis of Alzheimer’s disease (AD). Several findings indicate that the apolipoprotein E (APOE)-e4 allele is associated with high lipoprotein (a) [Lp(a)] levels and decreased levels of apolipoprotein A1 (apoA1), suggesting an increase in the susceptibility to AD [1]. Serum concentrations of Lp(a) have been found to be significantly higher in patients with vascular dementia [2] compared with those in healthy individuals. Moreover, plasma apoA1 [3] may be involved in Alzheimer’s disease. Nevertheless, the role of apoA1 and Lp(a) in AD remains unclear. We
tried to examine serum levels of apoA1 and Lp(a) in AD patients and we investigated any possible relationship of lipoprotein levels with cognition, activities of daily living and neuropsychiatric symptoms.

**Methods:** The population studied included 53 probable AD patients (21 men and 32 women with mean age of 74.2 ± 7.6 years). Sixteen patients were under treatment with Donepezil (10mg/day) and 37 were drug free. All patients were chosen from the Outpatient Clinic of the Geriatric Psychiatry Division, 1st Department of Psychiatry, Eginition Hospital. AD cases were diagnosed as having probable AD according to the criteria of the NINCDS-ADRDA and DSM IV (1994). Their cognitive function was assessed using Mini Mental State Examination (MMSE), the neuropsychiatric symptoms with Neuropsychiatric Inventory (NPI) and the activities of daily living with ADCS. Serum concentrations of apoA1 and Lp(a) were quantitatively determined using ELISA.

**Results:** The apoA1 and Lp(a) serum levels were respectively 442.9±97.9 and 36.5±31.7. Drug free AD subjects had higher serum level of apoA1 (460.5±97.3 versus 402.7±89.3, t =−2.02, p =0.04), but significantly lower levels of Lp(a) (48.07±32 versus 31.5±18.4, t =2.35, p =0.023) compared to AD patients treated with donepezil.

ApoA1, but not Lp(a), was significantly correlated with scores of global cognition and activities of daily living. These associations remained statistical significant after controlling for age and gender.

**Conclusion:** This study examined the association of lipoprotein levels with cognition, activities of daily living and neuropsychiatric symptoms in AD patients.

We found that AD patients with increased serum levels of apoA1 demonstrated better cognitive performance and better functioning in daily living, independently of age, sex and neuropsychiatric symptoms.

**References:**

**PP05 (ICGP Junior Investigator Awardee) | Depression and cognitive impairment among newly admitted nursing home residents in the United States**

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**Introduction:** Depression in older adults is common and is a major source of morbidity and mortality. Older adults with depression frequently present with cognitive impairment. Cognitive symptoms are associated with lack of antidepressant treatment response and increased risk of developing dementia. Little is known about the co-occurrence of these conditions among nursing home residents, a vulnerable but rapidly expanding population in the United States, despite the negative outcomes associated with these frequently co-occurring conditions. The objectives of this study were to: 1) describe the prevalence of depression and cognitive impairment among newly admitted nursing home residents; and 2) describe the treatment of depression.
**Methods:** We used Minimum Data Set (MDS) version 3.0 data from 2011-2013. The MDS is a comprehensive clinical assessment that is mandatory for all residents living in Medicare- and Medicaid-certified nursing facilities in the United States. MDS 3.0 contains more than 450 items on diagnoses, health conditions, treatments, and functional and cognitive statuses. We identified 4,196,686 nursing home residents with MDS assessments performed at admission during 2011-2013 who were 65 years of age or older, non-comatose, not admitted to a swing bed provider, and did not have delirium.

**Results:** Twenty-five percent (n = 1,059,617) of older adults had an active diagnosis of depression upon admission to a nursing home. Forty-six percent of these residents had cognitive impairment as measured by the Cognitive Function Scale. Of those with cognitive impairment, 54.7% had mild impairment while 5.3% had severe impairment. Approximately 20% of all residents had mild depression according to the staff-assessed PHQ-9, regardless of cognitive impairment status. One third of all residents with depression had a diagnosed comorbid anxiety disorder (33.0% of those with cognitive impairment, 33.1% of those without). Those with cognitive impairment were more likely to have dementia (42.1% vs 10.9%, p <0.0001) and to have had a cerebrovascular accident, transient ischemic attack, or stroke (16.0% vs. 10.2%, p<0.0001). Residents without cognitive impairment were more likely to have pain (70.7% versus 48.0%; p <0.0001). While almost one quarter of residents were receiving antidepressant medication (24.6% of those with cognitive impairment, 5.3% of those without), lack of psychological treatment was common and did not vary by presence of cognitive impairment (~48% of residents with depression). The prevalence of individual depression symptoms measured by the PHQ-9 did not vary by presence of cognitive impairment or antidepressant treatment status.

**Conclusion:** Many older adults have depression and some degree of cognitive impairment at admission to a nursing home. Despite the prevalence of depression in this population, antidepressant use is not common and does not differ by the presence of cognitive impairment. An enhanced understanding of the relationship between depression and cognitive functioning among older adults is necessary in order to properly treat both conditions and potentially prevent reduce the risk of developing additional disorders such as dementia.

**PP06 (ICGP Junior Investigator Awardee) | Molecular and neural basis of late life depression – Insights from animal study**


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**Background:** Late life depression (LLD) is a serious clinical disorder, whose symptoms differ from depression earlier in life, suggesting that the underlying mechanisms are also different. The present study used two mouse models of induced depression that provide translational models of two factors that are common in the elderly and may interact and contribute to the development of LLD. The chronic stress (CS) model mimics everyday life stressors, and bilateral carotid artery stenosis (BICAS) provides model for cardio-vascular insufficiency that is known to induce damage to the deep white matter. Exposing old and young female mice to these procedures followed by extensive behavioral battery enabled us to test the hypothesis that old mice are more susceptible to the hazardous effects of stress and vascular insufficiency.

**Methods:** CS: Mice were exposed to CS or control conditions for 5 weeks, after which they underwent extensive behavioral testing while continuing exposure to CS. VI: Common artery stenosis was induced using bilateral implantation of metal coils (0.22mm) around the carotid arteries. As late life depression
characterized by cognitive symptoms and residual cognitive impairment, the effects of chronic stress and vascular insufficiency on neuroplasticity, mainly manifested by neurogenesis, glial activation, and BDNF levels were tested.

**Results:** Old females were more vulnerable to the effects of chronic stress on weight than young mice. Two way ANOVA with repeated measures comparing change in body weight from baseline until after eight consecutive weeks of CS revealed a significant age by time interaction (F[2,58] = 11.126, p<0.01), and triple interaction of time, age, and exposure to CS (F[1,58] = 7.221, p<0.05) suggesting that only old mice exposed to CS significantly lost weight. Age by exposure interaction was demonstrated in the two cognitive tests used - novel object recognition (F[1,76]=4.373, p<0.05) and radial-arm water maze (RAWM) (F[1,74]=4.107, p<0.05), indicating that the cognitive functioning of young mice exposed to CS was higher compared with old mice. White matter lesions following BICAS were demonstrated histologically. Old VI mice also displayed longer RAWM latencies compared with young VI mice (age by treatment interaction F[1,29] = 7.318 p<0.05). Old mice also displayed lower levels of neurogenesis reflected by lower levels of doublecortin(F[1,12] = 120.45 p<0.0001) and synapsin (F[1,11] = 5.068, p<0.05). Although effect of stress and/or stress by CS exposure interaction were not demonstrated, it is plausible that lower hippocampal plasticity increased the vulnerability old mice to stress.

**Conclusions:** Chronic stress and vascular insufficiency, common precipitating factors for depression, anxiety, and cognitive decline, have differential effects depending on age. While old mice were susceptible in terms of developing behavioral and cognitive features often associated with LLD, young mice displayed striking resilience in both models. Such findings have key implications for a better understanding of debilitating symptoms that commonly occur in elderly individuals as well as their prevention and treatment.

**Funding:** Supported by a grant from the Israel Ministry of Science, Technology and Space in the context of the Japan-Israel Scientific Research Cooperation Program.

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**PP07 | Relationship between alcohol use disorder and cognition in the elderly**

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**Introduction:** The deleterious effects of alcohol on cognitive function were reported as early as 1880s by Wernicke and Korsakoff. Besides, the current literatures reflect developing understanding of effects and pathophysiology of alcohol on cognitive function.

The older alcoholics have been distinguished from the younger alcoholics with regard to impaired cognitive functioning in alcoholics, because the aging brain is more vulnerable to the toxic effects of alcohol than the younger brain. However, few studies have included samples of exclusively older subjects. This study aims to investigate the relationship between alcohol use disorder and cognition in Korean community-dwelling elderly, especially the gender-specific difference.

**Methods:** Data obtained from 1,274 subjects (1,083 men and 191 women) aged above 60 years was analyzed from the Gwangju Dementia and Mild Cognitive Impairment Study (GDEMCIS). All subjects completed the study questionnaire including demographic characteristics, history of current and past illnesses, drug history, Korean version-Mini Mental State Examination (K-MMSE) [1], and CAGE (cut down, annoyed, guilty feelings, eye-opener) [2].

We analyzed the general characteristics of participants grouped on the basis of alcohol use disorder via an analysis of covariance(ANCOVA) by regressing alcohol use disorder on K-MMSE as well as the interaction of alcohol use disorder and sex, after adjusting for age, educational level. SPSS software, version 12.0(SPSS Inc., Chicago, IL, USA) was used for all analyses.
**Results:** Of the total (mean age 72.1±6.1, mean educational level 6.7±4.6), 295 (23.2%) demonstrated alcohol use disorder (CAGE≥ 2) and 979 (76.8%) were non-alcohol use disorder. The mean of K-MMSE for alcohol use disorder group was 23.2±4.9, and for non-alcohol use disorder group was 23.7±3.9. In analysis of covariance, alcohol use disorder was associated with cognition. The mean of K-MMSE for female alcohol use disorder group was 20.2, and for female non-alcohol use disorder group was 22.6. The mean of K-MMSE for male alcohol use disorder group was 23.6, and for male non-alcohol use disorder group was 23.9. Interaction of alcohol use disorder and gender was also associated with cognition.

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*Table: Univariate analysis of variance of K-MMSE for the interaction of AUD and sex after adjusting for age, educational level*

AUD: Alcohol Use Disorder; K-MMSE: Korean version-Mini Mental State Examination

**Conclusions:** In conclusion, our study demonstrates an association between alcohol use disorder and cognitive impairment in the elderly. And especially the interaction of alcohol use disorder and gender was also associated with cognition.

**References:**

**PP08 | The relationship between temporal discounting and well-being in the elderly**

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**Introduction:** The "quality of life" concept is gaining importance in several fields of study including economics, sociology, social welfare studies, and medicine. The lengthening of life expectancy added importance to improving the quality of life for the elderly. There are many variables that affect elder generation's quality of life such as personal degree of subjective well-being, physical/psychological/social health, existence of a disease, area of residence, social status such as economic status and so on. Among those variables, the concept of temporal discounting has gained more attention recently. Temporal discounting means the ratio in which future compensation is converted to present compensation. This concept is built on the reasoning that most of the choices are intertemporal, and the future values are evaluated in a present basis. Therefore, the intertemporal comparison should be done by converting the future compensation to the present terms. This concept of temporal discounting is related with unwise decision making in health and economic status, thereby likely to lead to a decrease in the quality of life.
Aim: This study aims to examine association of temporal discounting with well-being of Korean community-dwelling elderly.

Methods: Among 5,621 elderly individuals, research subjects were limited to those who were able to understand the questionnaires and communicate. However, the following were excluded from the sample: subjects who recorded above 3 in Hoyl Five-item version of the Geriatric Depression Scale; subjects diagnosed with dementia and in treatment; subjects with serious physical illness. Finally, the subjects of this research were 4,373 community-dwelling older persons. Each subject was administered the questionnaires regarding the socio-demographic characteristics, temporal discounting which was measured using standard questions in which participants were asked to choose between an immediate, smaller payment and a delayed, larger one. Outcome variable is Korean version of the WHO Five Well-Being Index (WHO-5). Statistical analyses including the Pearson's correlation test and logistic regression were performed in this study. Logistic regression was applied on WHO-5 Index's subscales in the same manner as well.

Results: At baseline, temporal discounting was negatively associated with WHO-5 in the Pearson's correlation test ($r=0.04$, $p=0.006$). In adjusted model for confounding variables, temporal discounting was negatively associated with WHO-5 (Odd ratio(95% CI.)=$0.57(0.35-0.92)$, $p=0.021$). Temporal discounting rate's relations with WHO-5 Index's energy subscale (OR = 0.72, $P = 0.074$) found out to be statistically insignificant, but its relations with anxiety subscale (OR = 0.45, $P <0.001$,) and positive well-being subscale (OR = 0.56, $P = 0.002$) showed statistical significance.

Conclusions: Among elderly individuals without a significant symptom of depression and a decrease in cognitive function, this research was able to identify a negative correlation between subject's temporal discounting and their quality of life. Examining subscales of WHO-5 Well-Being Index, the research finds that the decrease in the quality of life was more closely associated with anxiety and positive well-being rather than the energy subscale.

References:

PP09 | Trends and correlates of in-patient initiation of antipsychotics among elderly patients discharged to nursing homes
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Introduction: In the United States, high antipsychotic use persists in nursing homes despite black boxed warnings from the Food and Drug Administration and prescribing regulations from the Centers for Medicare and Medicaid Services. Nearly half of nursing home residents on antipsychotics initiate therapy before the nursing home admission. Estimates of initiation in hospital settings are scarce.

Objectives: To estimate trends in in-patient antipsychotic use among elderly patients and to identify correlates of initiation among elderly patients discharged to nursing homes
Methods: Using an extract from the United States Cerner HealthFacts database, we identified 297,127 hospitalizations from 189,225 unique patients aged ≥ 65 years without schizophrenia, Tourette’s syndrome, or Huntington’s disease discharged from 104 hospitals in the United States to nursing homes between 2000 and 2012. We estimated prevalence of antipsychotic use on day of hospital admission and among those without an antipsychotic medication record on the day of admission, the proportion with a medication record for an antipsychotic later in the hospital stay. A random effects logistic model was used to test for trends while adjusting for clustering of patients within hospitals. Correlates of initiation of use at the patient-level (e.g. age, sex, race, diagnoses) and hospital-level (e.g. teaching hospital, bed size) were determined using hierarchical models.

Results: On the day of admission, 15.3% received an antipsychotic (13.7% in 2000, 19.7% in 2007, 12.6% in 2012). In 2012, haloperidol was most commonly prescribed (46.9%), followed by quetiapine (18%), and risperidone (10%). Nine percent initiated an antipsychotic during their hospital stay (17.1% in 2000 and 6% in 2012; (p for monotonic trend < 0.0001); 2012 hospital specific estimates ranged from 0% to 15.4%). Once initiated, 70% had antipsychotics orders on the day of hospital discharge. Women were less likely than men to have antipsychotics initiated (Odds Ratio (OR): 0.76; 95% Confidence Interval (CI): 0.69-0.83). Patients with delirium were at greatest risk for initiation (OR: 7.78; 95% CI: 6.56-9.21). The estimated variance of the hospital intercepts was 0.17 (standard deviation: 0.05) indicating a significant hospital effect on antipsychotic initiation. Bed size of the hospital facility was the strongest observed facility-level correlate of antipsychotic initiation (e.g. OR<99 beds versus >500: 0.37; 95% CI: 0.24-0.57).

Conclusions: Antipsychotic use was prevalent at admission, and commonly initiated among elderly inpatients. Estimates varied by hospital suggesting that hospitals (as the point of initial prescribing of antipsychotics) may offer a new target for intervention. The CMS efforts to develop a hospital-based quality indicator to address the concern of initiation of antipsychotics in hospital are warranted.

PP10 | Clinical, cognitive and neurochemical profile of patients with cerebral amyloid angiopathy: A case-series

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Introduction: Cerebral Amyloid angiopathy (CAA) is a rare neurovascular disorder characterized by amyloid accumulation in the small cerebral arterial vessels. Lobar intracerebral haemorrhage is the hallmark, but microhaemorrhages and subcortical ischemic lesions may also present, resulting in focal neurological deficits, seizures, cognitive impairment and psychiatric implications. In this case series, we aim at discussing aspects of CAA that might also be relevant to psychiatry.

Methods: We retrospectively collected data of six patients (3 males, 3 females) presenting one or more major cerebrovascular events (CEs) and meeting the Boston Criteria for probable CAA. They were admitted in the 1st Neurological Department of the National and Kapodistrian University of Athens, in a period between 2013 and January 2015. All patients had a detailed diagnostic assessment, including clinical and neuropsychological investigations (MMSE, FAB, CLOX, and 5W), CSF biomarker, and MRI scans.

Results: Four of six patients had psychiatric symptoms such as depression, delusions, misidentification syndrome; sleep disorders (RBD-like). Cognitive decline was associated with memory impairment (4/6), visuospatial difficulties (4/6) and lower perceptual speed (3/6) and frontal impairment (3/6). In all of them, axial GRE MR image showed typical multiple cortical-subcortical microbleeds. Their CSF biomarker profile was compatible with AD in 4/6, one had a marginal and inconclusive profile and 1 had “amyloid only” profile.
Conclusion: Cognitive as well as behavioral and psychiatric symptoms are common in CAA. These aspects represent possible psychiatric implications of CAA and suggest that CAA is a disease with relevance to psychiatry.

PP11 | Neuropsychiatric profile of patients with Parkinson’s disease dementia, dementia with Lewy bodies and Alzheimer’s disease: A case-control study

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Introduction: Behavioral and Psychological symptoms (BPSD) are common manifestations of Parkinson’s disease dementia (PDD), Dementia with Lewy bodies (DLB) and Alzheimer’s disease (AD). The aim of this study was to compare the BPSD among PDD, DLB and AD patients.

Methods: We conducted a retrospective case-control study which included 19 PDD, 28 DLB and 19 AD patients with comparable age, education, disease duration and dementia severity. All patients were admitted in our Department between January 2013 and January 2015. Neuropsychiatric symptoms were assessed with the Neuropsychiatric Inventory (NPI), while cognitive function was assessed with the Mini-mental State Examination (MMSE). For global severity of dementia, assessed Clinical Dementia Rating scale (CDR) was used.

Results: The PDD group was similar to AD group, in NPI total score, the use of antipsychotics and agitation, but both differ significantly from the DLB group, which was more severely affected. Groups did not differ among each other in the subscores of delusions, depression, euphoria, disinhibition and appetite. Hallucinations showed the highest scores in both DLB and PDD, and were statistically different from AD. Aberrant motor behavior (AMB), agitation and anxiety were more severe in DLB vs. PDD. Sleep parameters were more severely affected in DLB and PDD vs. AD. Patients with DLB were 81% more likely (OR = 0.19; p < 0.0001) to use antipsychotics compared with AD, after adjusting for demographic covariates, CDR scores and NPI subscores (disinhibition, depression, hallucinations, anxiety, agitation and delusions). Hallucinations (OR=1.7 95% CI 1.13–1.12) and agitation (OR=2.4 95% CI 1.17–5.00) were associated with antipsychotic use.

Conclusion: Total NPI scores, anxiety, agitation and AMB parameters were less severe in PDD vs. DLB with the former being comparable to AD group. Hallucinations and sleep disturbances were almost similarly affected in PDD and DLB. However, PDD seems intermediate between AD and DLB, but more close to AD in most parameters.

PP12 | Predictive factors associated with psychological symptoms of the caregivers of people with dementia in Japan: Cross-sectional study

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Introduction: Caregivers of people with dementia are likely to have health problems, including mental health problems such as depression. The objective of this study is to examine predictive factors associated with depressive symptoms of the caregivers of people with dementia in Japan.

Methods:
Design: Cross-sectional study.
Sample: 1,437 patient-caregiver dyads enrolled in the informal care time study as a part of the study of estimating the cost of dementia in Japan.

Analysis: Bivariate and multivariate regression analysis was conducted in order to evaluate predictable factors associated with caregivers' Kessler's Psychological Distress Scale (K6) score.

Results: 82% of the caregivers scored higher than 4 in K6 and 18% of the caregivers scored higher than 12. According to the results of logistic regression analysis (cut-off 5), mental and physical symptoms of patients, informal care time, caregivers’ living with patients with dementia, number of caregivers and nursing care level associated K6 score. According to the results of logistic regression analysis (cut-off 13), mental and physical symptoms of patients, sex of caregivers, informal care time, marital status of caregivers and number of caregivers associated K6 score.

Conclusion: This is one of the largest studies analyzing the multiple predictors of depression in the caregivers of the people with dementia in Japan. We confirmed two things, which are in accordance with the results from previous studies. One is that the prevalence rate of the psychological symptoms of the caregivers is quite high. And the other is BPSD (Behavioral and Psychological symptoms of Dementia) is surely associated with caregivers’ psychological symptoms.

PP13 | Sleep quality in carers of demented patients: The impact on carers' health status and functionality
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Introduction: Recent research findings have revealed that almost 2/3 of demented people carers suffer from a sleep disorder. These sleep disturbances are associated with severe changes in carers’ sleep routine, cause multiple somatic, psychological, social and economic problems and determine the overall carers’ quality of life [1]. This literature review describes the main characteristics of these sleep disorders, clarify their multiple implications in carers’ health and functionality, and summarize the current therapeutic options.

Methods: A search was conducted on Pubmed using the following keywords: “Sleep”, “Dementia”, “Carers and/or Caregivers”. Twenty-four articles (literature reviews and research protocols), written in English and published in peer-reviewed journals, were retrieved, evaluated and reviewed.

Results: Female gender, older age, anxiety disorders and bereavement were the main predisposing factors to develop sleep disturbances among Alzheimer carers. Alzheimer carers had different sleep architecture (less proportion of their sleep in restorative sleep stages, increased sleep latency, multiple shifts between sleep stages) compared to non-caregivers whereas Frontotemporal Dementia carers used sleep medications more frequently. The most common profiles of carers were people with a high medical morbidity (hypertension, high blood cholesterol, diabetes, obesity) which mainly suffered from sleep apnea and restless legs syndrome [2,3]. Chronic fatigue, reduced quality of care services, difficulty in decision making, propensity to accidents were some of the most important long-term implications in caregivers’ health and functionality [2]. There are multiple therapeutic options such as medications (a great variety of antidepressants and sleep inducing agents), psychotherapy, yoga and physical exercise [1].
Conclusion: The above-mentioned findings underline the need for further research on this topic in order to improve carers’ sleep quality and overall quality of life, a fact which would be beneficial not only for caregivers but also for the demented patients.

References:

Source of Funding: None

PP14 | The relation between REM sleep behavior disorder and Parkinson’s disease
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Introduction: REM Sleep Behavior Disorder (RBD) is a unique, rare parasomnia characterized by dream enactment behavior and is frequently found in Parkinson’s disease (PD). RBD may represent the first feature of neurodegeneration and can be an early marker for these diseases, especially for PD [1]. This review describes the main epidemiological, clinical, pathophysiological and therapeutic features of RBD concentrating into its association with PD and emphasizing their common neuropathophysiological patterns and the implications as well as the specific characteristics of their comorbidity.

Methods: A comprehensive review of the literature was conducted through Pubmed and Google Scholar databases using the following keywords: “Parkinson’s Disease”, “REM Sleep Behavior Disorder”, “Sleep Disorders”, “Parasomnias”, “Epidemiology”, “Pathophysiology”, “Clinical manifestations”, “Clinical subtypes”, “Comorbidity”. A literature search was undertaken for articles published through the last thirty five years. The studies considered eligible were literature reviews, research protocols and case reports written in English and published in peer-reviewed journals. Finally 100 articles were included in this review.

Results: The prevalence of RBD has been estimated at 0.38% of the general population, while concentrating on RBD prevalence in PD, this was estimated at 15%. RBD may precede development of motor symptoms of PD and other synucleinopathies by a number of years or decades in 18-22% of patients [1]. Recent studies have suggested that RBD in PD is associated with increased cognitive impairment, severe autonomic dysfunction and specific motor manifestations, implying a common pattern of neurodegeneration. Indeed, data come from numerous pathological, pathophysiological and neuroimaging studies corroborate closely related, neuropathophysiological aspects of each of the two disorders [2]. As regards the treatment of RBD in PD there is a majority of well tolerated as well as future promising pharmaceutical and invasive therapies [3].

Conclusion: According to epidemiological, pathophysiological and clinical data RBD and PD are closely interconnected. The fact that these two disorders sharing common pathological, neuroimaging and neurophysiological abnormalities, in combination with a distinct clinical phenomenology in PD associated with RBD and regarding the treatment implications in PD-RBD comorbidity, suggest that there is a difference between the neurodegeneration patterns of PD patients with RBD and PD patients without RBD and give us new insight into the progress and treatment of both of the diseases.
Introduction: Pain is a complex psychological and neurophysiological phenomenon and has been shown as an onset symptom of Parkinson’s disease (PD) occurring even before motor symptoms. Patients with PD report a variety of pain-related symptoms, which severely impair their quality of life and frequently remain underdiagnosed and undertreated [1]. The aim of this review is to describe the epidemiological, clinical, and therapeutic features of pain syndromes in PD patients and to clarify their pathophysiological basis according to latest research findings.

Methods: An extensive search in Medline was conducted using the keywords “Pain” and “Parkinson’s Disease”. Literature reviews, research protocols and case reports written in English and published in peer-reviewed journals between 1990 and 2016 were retrieved. Data concerning epidemiology, pathophysiology, clinical manifestations and treatment of pain syndromes in PD patients were extracted. Finally 119 articles were included in this review.

Results: Prevalence of pain in PD patients varies between 40% and 83% and the two main types of pain are the nociceptive and the neuropathic one [1]. The pathophysiological mechanisms underlying pain related to PD in humans remain unclear and only indirect evidence suggested nociceptive system dysfunction in these patients. The main pathophysiological theory is that abnormal basal ganglia function in PD modulates pain directly by increasing or diminishing nociceptive signal propagation, and indirectly by influencing affective and cognitive processes thereby regulating how patients expect, experience and interpret nociceptive signals and pain [2]. The treatment of pain in PD is based mainly on empirical data. The pharmacological management includes a variety of antiparkinsonian, antinociceptive and antineuropathic medications. Deep brain stimulation (DBS) targeted to the subthalamic nucleus and globus pallidus effectively relieves various types of PD-related pain, such as musculoskeletal, dystonic and central Parkinson pain [3].

Conclusion: Pain is a core non-motor symptom of PD with unclear pathophysiology, multiple clinical types and different responses to treatment. With the above in mind, future studies are needed in order to have a better understanding of this phenomenon and improve care provided to patients.

References:

Source of Funding: None
PP16 | Relationship of neuropsychiatric symptoms of Alzheimer’s disease and driving behavior


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Introduction: A significant percentage of patients diagnosed with Alzheimer’s disease (AD) continue to drive and a wide number of studies have shown impaired driving behavior with increased accident risk. Moreover, the majority of patients with AD suffer from neuropsychiatric symptoms, even in the beginning of the disease. Thus, their driving could be possibly affected by these neuropsychiatric symptoms. The objective of this study is to investigate the relationship between neuropsychiatric symptoms and driving ability in patients with mild AD, with the use of a driving simulator.

Methods: 23 participants diagnosed with mild AD (mean age=74.9 years ± SD=7.4, mean driving experience=43.6 years ± SD=10.1) and 32 healthy individuals (mean age=64.3 years ± SD=6.9, mean driving experience=38.2 years ± SD=5.9) participated in a driving simulator experiment. The driving experiment included two conditions: a) rural road with low traffic volume and b) rural road with high traffic volume. In addition, the participants underwent a detailed neurological and neuropsychological examination.

Results: T test analysis showed that in comparison to the control group, patients with AD had a significantly worse performance in the driving task. Moreover, the linear regression model showed the following: a) apathy and depression predicted increased reaction time to unexpected events, b) lack of initiative, apathy and irritability predicted increased accident probability and c) anxiety and lack of initiative predicted increased headway distance. Finally, AD patients with neuropsychiatric symptoms such as apathy, depression and lack of initiative appeared to have a significantly worse performance in reaction time to unexpected events, accident probability and average speed, when compared to AD participants without those symptoms.

Conclusion: Our findings indicate that the presence and severity of neuropsychiatric symptoms, especially apathy and depression, affect driving performance of patients with mild AD and may constitute important risk factors for impaired driving behavior. To our knowledge, this is the first study that associates driving ability with neuropsychiatric symptoms.

Acknowledgment: The present study was performed in the framework of the research project DriverBrain entitled “Analysis of the performance of drivers with cerebral diseases”, concerning the driving skills of individuals with Alzheimer’s disease, Parkinson’s disease, and Mild Cognitive Impairment (“Driver Brain,” 2012).

PP17 | Hashimoto encephalopathy; a rare cause of dementia not to be missed

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Introduction: Dementias generally develop slowly, allowing physicians to evaluate patients in an outpatient setting. Rapidly progressive dementias (RPDs) develop subacutely over weeks or rarely acutely over days. In contrast to most dementing conditions due to degenerative disorders that take years to progress to death, RPD can be quickly fatal. It is critical to evaluate the RPD patient without delay as some of them may have a treatable condition.
Most referrals are related to a potential diagnosis of Creutzfeldt-Jakob disease (CJD), but there is a need for a broader diagnostic approach to RPD since 15-20% of referrals are due to other non-prion conditions, many of which are treatable.

**Clinical Description:** We report the case of an 86-year-old woman who developed subacutely over a week, gait imbalance that led to several falls, apathy, slowness in performing daily activities, apraxia, dysphasia, attention deficit and amnestic episodes. She had no motor or sensory deficits. Her past medical history included arterial hypertension, hypercholesterolemia, thrombophilia, echinococcus cyst. A CT scan revealed nothing more than mild atrophy excluding subdural hematoma, hydrocephalus or other brain occupying lesions. She was started at low doses of levodopa and rivastigmine, assuming that she suffered from dementia underdiagnosed, that due to an unknown factor (emotional stress, dehydration, flu or other) was revealed giving the misperception that was sub acutely developing. The patient although in treatment was continuously deteriorating. MRI could not be performed. Electroencephalography (EEG) showed generalized slow waves with diffuse cortical dysfunction, without any epileptiform discharges. The patient denied lumbar puncture. Electrolytes, the serum anti-nuclear antibodies, rheumatoid factor, and anti-DNA screening were negative. Thyroid function tests were normal, but the anti-thyroid antibodies for thyroperoxidase and thyroglobulin were elevated. Given the indications for Hashimoto's encephalopathy, she was subsequently started on prednisone 60 mg orally per day. The patient's clinical improvement was impressive and her neuropsychiatric symptoms resolved in a week.

**Discussion:** Hashimoto's encephalopathy (HE) is a rare, steroid-responsive autoimmune disease characterized by symptoms of acute or subacute encephalopathy. Thyroid autoantibodies are elevated in all patients and this is required for a diagnosis although there is no clear relationship between the severity of neurologic illness and serum concentration of antibody titers. Glucocorticoids are the mainstay of therapy. In treated adults, the prognosis of HE is good, with 90% of the patients in remission after 10 years.

**Conclusion:** The evaluation of patients with rapidly progressive neurologic symptoms and cognitive and psychiatric problems can be challenging. More common causes of encephalopathy should be excluded, such as infection, electrolyte imbalance, metabolic disease, toxins, neoplasm, vasculitic syndromes and autoimmune encephalopathies (paraneoplastic and non-paraneoplastic). Clinicians should consider Hashimoto's encephalopathy in patients with unexplained encephalopathy or rapidly progressing dementia. Elevated serum levels of anti-TPOAb and TgAb's coupled with a marked response to corticosteroids is diagnostic. Hashimoto's encephalopathy should be considered in the differential diagnosis of encephalopathies of unknown cause or rapidly progressing neurodegenerative disorders because it is treatable and often has a favorable prognosis.

**PP18 | Neuropsychological profile of depressive subtypes: Melancholic-psychotic depression**


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**Introduction:** Several studies have dealt with the neuropsychological profile of depression and cognitive deficits connection with biomarkers, such as cortisol. The findings support the hypothesis of the circuit malfunctioning basal ganglia-prefrontal cortex. In this study we investigated the differences in memory and executive functions in patients with major depressive disorder (MDD), in relation to the existence of melancholic or psychotic elements.
Material and Methods: Seventy patients with MDD, twenty of whom had melancholic, twenty had non-melancholic, thirty of which had psychotic features and twenty healthy controls, of similar age and educational level, were examined using neuropsychological tests of the Cambridge Neuropsychological Test Automated Battery (CANTAB). The tests were designed to examine memory (Paired Associates Learning-PAL and Spatial Recognition Memory -SRM) and executive functions (Stockings of Cambridge -SOC and Intra-Extra Dimensional Set Shift -IED).

Results: Depressed patients in total, compared to controls showed statistically significant deficits both in memory and executive functions. The melancholic patients showed differences from the non-melancholic in executive functions that require set shifting (IED) and memory tasks that require learning (PAL). The patients with psychotic depression had almost similar performance with the melancholic patients with a trend to perform worse.

Conclusions: Neuropsychological deficits in depressed patients more related to executive functions and less memory. The model of dysfunction of the cingulate (dorsal part) and prefrontal cortex (dorsolateral) was supported. For patients with melancholic or psychotic features seems to be a quantitative difference in general and a qualitative difference in set shifting. The latter finding is considered to be associated with further impairment of the ventral cingulate and orbitofrontal cortex.

PP19 | Cerebrospinal fluid biomarkers in the differential diagnosis of dementia
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Introduction: Alzheimer’s disease (AD) is the primary cause of dementia and comprises the most common and frequent type of dementia. Vascular factors are thought to contribute to the development of disease pathology in neurodegenerative dementia [1]. Vascular dementia (VaD) comprises a group of dementia patients having various vascular diseases especially in the elderly population. Despite existing criteria, differential diagnosis of VaD and AD remains difficult [2]. Cerebrospinal fluid (CSF) biomarkers have been proven to provide a promising diagnostic value in many neurodegenerative disorders [3]. Several findings indicate higher levels of beta amyloid 1-42 (Aβ1-42) and lower levels of Tau-protein in VaD than in patients with AD [4-5]. The aim of our study was to figure out if selected CSF markers (tau protein and Aβ1-42) that may help to distinguish between Alzheimer’s disease and vascular dementia. Simultaneously, we analysed the levels of investigated markers in regard of the severity of Alzheimer’s disease.

Methods: We analysed the CSF levels of tau protein and Aβ1-42 from 70 patients (38 women and 32 men with the mean age 82±9.9 years). 37 (52.8%) patients were diagnosed with Alzheimer’s disease, from this group 11 (15.7%) patients were in early stages of AD, 17 (23.6%) were diagnosed with vascular dementia (VaD) and 16 (22.9%) had no cognitive impairment. CSF tau-protein and Aβ1-42 concentrations were determined using ELISA. As variables, except for age, were not normally distributed, nonparametric analyses were used to compare different groups.

Results: Patients with AD including patients in early stages of AD as well as patients with VaD demonstrated significantly higher CSF tau level as compared to controls (p<0.001, p=0.01 and p<0.001, respectively).
A significant lower CSF levels (p<0.001) of Aβ\(_{1-42}\) in AD as compared to VaD patients were observed. That significance for lower Aβ\(_{1-42}\) levels was recorded in early stages of AD (p=0.011) compared to VaD group as well. Furthermore, patients in advanced AD stages showed higher tau levels (p<0.001) as those in early stages of AD. No differences between CSF marker levels and gender were found.

**Conclusion:** Our results confirm previous studies suggesting that tau protein levels are helpful indicator of the presence of neuronal degeneration \[5\]. The decreased level of Aβ\(_{1-42}\) was observed in AD patients compared to VaD patients even in the early stages of AD suggesting its practical utility in the differential diagnosis of these entities. Moreover, the measurement of various CSF markers might be potentially useful in the early diagnosing of various dementia disorders.

**References:**

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**PP20 | Gender differences in senile depression. Ilion Municipality Hellenic Study (IMHS)**

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**Introduction:** Depression is a disorder with a high prevalence in the older individuals. Specific genotypic expressions, loneliness, various types of loss, cognitive decline, and psychosocial difficulties are commonly considered as risk factors. Also, the female gender is steadily related to accentuated risk for the development of depression.

**Scope:** (a) estimation of the frequency of depressive symptomatology in female and male older individuals, (b) exploration of the role of psychosocial factors on the development and severity of depressive symptomatology, and (c) detection of differences on the patterns of depressive symptomatology according to gender.

**Methods:** A cross-sectional study with the inclusion of 358 participants above the age of 60 years old was conducted. Females and males were evenly balanced according to age. All participants were community-dwelling older adults. The Geriatric Depression Scale (GDS) was applied for the evaluation of depressive symptomatology.

**Results:** The odds ratio of females to males for the development of depressive symptomatology was 1.81. Five percent of males and 6.7% of females have GDS scores that indicate moderate to severe depressive symptoms, whereas 16.8% of males and 26.8% of females have GDS scores that indicate mild to moderate depressive symptoms. The chi-square test for independence showed in the case of males that mild to moderate depression was significantly associated with age, education, traumatic experiences and
marginally with living alone. In the case of females significant associations were observed with physical exercise and the presence of grandchildren. Finally, moderate to severe depression was associated in the group of females with the amount of leisure activities. At a qualitative level, males where characterized at a greater extent by feelings of hopelessness whereas females by apathy.

**Conclusion:** The greater frequency of depressive symptoms in the older females compared to males could be explained, apart from gender-related biological differences, by sociocultural factors that prevent women from achieving mastery and high levels of self-worth, thus leading to dependency, low self-esteem and finally to the development of depression. The detection of various protective and risk factors as concern the presence of depressive symptomatology might add to the existing knowledge and facilitate the application of effective intervention programs that focus on improving the psychosocial health of older adults.

**PP21 | Exploring the association between depression and major neurocognitive disorder**

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**Introduction:** Mood disturbances as well as impairment in memory and other cognitive functions are commonly observed in older individuals. Contrary to the cases where these clinical conditions appear independently, the diagnostic process is complicated and full of obstacles in cases where depressive symptoms are interwoven with cognitive impairments.

**Objectives:** (a) Exploring the association between mood disturbances and cognitive impairments, as assessed by the scales GDSsf and MMSE; (b) exploring the role of socio-demographic variables on the levels of depression and cognitive impairment; and (c) exploring for possible associations between the underlying factors of the scales GDSsf and MMSE

**Methods:** Cross-sectional study that included 531 participants (age >60 years old, Mean =72.3±6.4 years) living independently in an urban region. The ratio of female to male participants was 1.7. The vast majority of the participants had received only primary education ≤6 years (79.1%).

**Results:** Among the participants with major neurocognitive disorder (DSM-5/ 2013) the 38.7% seem to have also depression, while among the participants with depression the 34.3% seem to have also major neurocognitive disorder. Age, education, family status and the solely living appear to influence the scores of the participants in both scales. The MMSE score is negatively correlated with dysphoria, apathy, hopelessness and memory factors of the GDSsf scale. Similarly, the GDSsf score appears to be negatively correlated with place orientation, calculating, recall and praxia factors of the MMSE.

**Conclusions:** The present findings support the presence of a link between major neurocognitive disorder and depression. The clinician need to assess for depressive symptoms in cases of major neurocognitive disorder as well as to screen for cognitive impairment those older individuals that have a diagnosis of depression. A broader clinical evaluation can facilitate the accuracy of the diagnosis and therefore improve the quality of the treatment that is provided to the target population of the advanced agers.
**PP22 | Autoimmune and paraneoplastic encephalitis presenting with neuropsychiatric symptoms. A case-series report**

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**Introduction:** Autoimmune and paraneoplastic encephalitides are immune-based CNS diseases that manifest with diverse symptoms, such as cerebellar ataxia, autonomic dysfunction, movement disorders, sleep disorders, cognitive impairment and neuropsychiatric symptoms. Occasionally neuropsychiatric symptoms predominate and differential diagnosis with psychiatric diseases becomes problematic.

**Methods:** We present 4 patients with diverse autoimmune or paraneoplastic encephalitides (an anti-NMDA-R, an anti-Caspr2, an anti-CRMP5 and an anti-GAD) and prominent neuropsychiatric symptoms. We describe the specific clinical manifestations of each encephalitis, their natural history, as well as detailed information on their neuroimaging, neurophysiological and biochemical profiles. We concentrated on the data that assisted in their differential diagnosis from psychiatric disorders.

**Results:** The anti-NMDA-R patient presented with manic-like manifestations (ideas of grandiosity, hypersexuality, inhibition loss) followed by acoustic hallucinations and delusions. The anti-Caspr-2 patient exhibited severe irritability with pronounced suspiciousness and delusions of persecution. The anti-CRMP5 patient had fluctuating depressive symptoms with suicidal ideation and mood congruent delusions. Finally, the anti-GAD patient had aggression, irritability and delusions (mainly with jealousy). All patients had natural courses atypical for a psychiatric disorder. Furthermore, their neurologic examination and laboratory profile assisted in the correct diagnosis.

**Conclusion:** Immune-based encephalitis can present with psychiatric manifestations. Atypicalities in natural history and presence of neurological signs at examination should prompt further investigations to exclude an underlying neurological disorder. Since these disorders are potentially reversible, psychiatrists should become familiar with their diagnosis and appropriate therapeutic options.

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**PP23 | Neuropsychiatric inventory subscale analysis in patients with Parkinson-plus syndromes**

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**Introduction:** Parkinson plus syndromes are a heterogeneous group of 3 neurodegenerative akinetic-rigid extrapyramidal diseases (multiple system atrophy, corticobasal degeneration and progressive supranuclear palsy), with otherwise distinct clinical features, which occasionally include neuropsychiatric symptoms. The Neuropsychiatric Inventory (NPI) is a useful tool for quantifying neuropsychiatric symptoms. It consists of 12 items, which can be categorized in 4 major subscales, namely the Affective (containing the depression and anxiety items), the Psychosis (containing the delusions, hallucinations and nigh disturbances items), the Apathy (containing the apathy and food disturbance items) and the Hyperactivity (containing the aggression, irritability and disinhibition items) Subscale.

**Methods:** We implemented the NPI in 38 patients with a diagnosis of probable Parkinson-plus syndrome (13 CBD, 10 MSA, and 15 PSP). We analyzed the NPI subscales' scores in the 3 groups, in order to study possible differences in neuropsychiatric symptomatology and their importance in the differential diagnosis of a patient with probable Parkinson-plus syndrome.
Results: The groups differed in their Total NPI Score (p=0.008) and in the Apathy Subscore (p<0.0001). Post-hoc analysis revealed that MSA patients had significantly lower Total NPI scores compared to PSP patients (p=0.006). PSP patients had significantly higher Apathy Subscores compared to both MSA (p<0.001) and CBD patients (p=0.006).

Conclusion: Patients with Parkinson-plus syndromes differ in the severity and frequency of neuropsychiatric symptoms. These symptoms are rare in MSA and frequent in PSP, and usually present as apathy and food disturbances.

PP24 | Driving performance and MCI: The influence of neuropsychiatric symptoms  
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Introduction: Considering that individuals with Mild cognitive impairment (MCI) are at high risk of developing dementia [1], their driving performance and safety have provoked great concerns. Neuropsychiatric symptoms (NPS) are common features in MCI [2]. Therefore, the objective was to examine the prevalence of NPS and whether they can predict a problematic driving performance among the MCI population.

Methods: 31 patients with amnestic MCI multiple domain (age=70.9±9.4) participated in a driving simulator experiment which included a rural and an urban road, under low and high traffic. Basic driving parameters were tested: the average speed in km/h, the distance from the ahead driving vehicle in meters, the frequency of engine’s deactivation, the average reaction time towards an unexpected incident in msec and the accident probability (%). The NPS were evaluated with the Neuropsychiatric Inventory (NPI) and the depressive symptoms with the Patient Health Questionnaire (PHQ-9).

Results: The most frequent symptoms were irritability (52%), depression (45%), anxiety (45%), apathy (23%), aggression (23%) sleep disturbances (19%) and 26% mild-moderate depressive symptoms. Simple regression models were applied in order to examine the capacity of various NPS to predict the driving measures. In the rural area, depression [R²=.243, F (1, 22) = 7.079, p<.05] and irritability [R²=.17, F (1, 22) = 4.69, p<.05] predicted the sudden deactivation of the engine, whilst PHQ-9 predicted the average speed [R²=.200, F (1, 20) = 5.02, p<.04]. In urban road and low traffic, depression [R²=.184, F (1, 21) = 4.74, p<.05], anxiety [R²=.251, F (1, 21) = 7.05, p<.05], sleep disturbances [R²=.172, F (1, 21) = 4.37, p<.05] and PHQ-9 [R²=.483, F (1, 19) = 17.75, p<.001] also predicted the deactivation. In high traffic, depression [R²=.242, F (1, 18) = 5.75, p<.05], anxiety [R²=.443, F (1, 18) = 6.30, p<.005] and PHQ-9 [R²=.356, F (1, 17) = 9.40, p<.01] predicted the average reaction time. Multiple regression analysis showed the unique contribution of anxiety, sleep changes and PHQ-9 [R²=.703, F (2, 20) = 13.39, p < .001] to the increased deactivation of the engine, in the urban road with low traffic. At last, PHQ-9 was the only predictor of the increased average reaction time [R²=.356, F (1, 17) = 9.40, p < .01], in the urban settings under high traffic.

Conclusions: The severity of NPS in MCI might be a contributing factor of a poorer driving performance, especially under more demanding environmental settings, such as the urban road. The results suggest a more detailed evaluation of the psychopathology in MCI patients in order to reflect the severity of symptoms and their impact on driving behavior, as risk factors. Individualized interventions must be
applied especially in the stage of MCI, in order to improve their driving behavior before progressing to
dementia.

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**References:**


**PP25 | Severity of extrapyramidal side effects in elderly patients treated with antipsychotic medication: A basal ganglia imaging study**

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**Introduction:** Antipsychotic medication (APM) is associated with the development of subacute reversible extrapyramidal side effects (EPSE) in elderly patients and severe movement disorders [1-2]. Differentiating Drug Induced Parkinsonism (DIP) from Parkinson’s disease (PD) may be a challenge to clinicians considering that discontinuation of the neuroleptic agent in DIP, should relieve the symptoms of parkinsonism [3]. The aim of our two-years prospective study was the severity of EPSE and its relationship with the basal ganglia functional anatomy assessment in elderly patients who were treated with antipsychotics.

**Methods:** This is a prospective interventional non comparative case series. 13 elderly inpatients (9 (69.2) female, 4 (30.8%)male, mean age 79 (SD: 5.84). 13 patients, with variable psychiatric diagnoses, had been on antipsychotic medication for at least one year prior to their current admission and presenting EPSE of different severity. 24 month was the timeframe between antipsychotic withdrawal and evaluation of parkinsonism. They were all administered the MMSE and the Simpson- Angus scale for the cognitive function and EPSE evaluation respectively. All patients underwent to I-123 ioflupane single-photon emission computed tomography (DaTscan) for the assessment of the basal ganglia’s presynaptic dopamine function and visually assessed by two raters, blinded to the clinical diagnosis, according to the Benamer’s criteria.

**Results:** 5 patients with a normal I-123 ioflupane single-photon emission computed tomography (DaTscan) study developed reversible EPS and 2 patients with abnormal grade 3 study developed Parkinson disease. 2 (50%) patients with abnormal tracer uptake with moderately asymmetric dopaminergic loss (grade 2) and 1 (50%) with abnormal tracer uptake with moderately asymmetric dopaminergic loss (grade 1) developed Irreversible EPS. Both patients who developed Parkinson disease died during follow up.

**Conclusions:** The development of irreversible EPSE and negative clinical outcome was observed in patients with abnormal basal ganglia imaging who were treated with antipsychotic. We recommend that I-123 ioflupane single-photon emission computed tomography (DaTscan) DaTscan could be a valuable imaging method in preventing negative clinical outcome in elderly patients treated with antipsychotics by providing a differentiation of DIP from PD.
PP26 | Religious behaviors in dementia: Neuroimaging correlates

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Introduction: Religious behavior is a uniquely human phenomenon, present in all cultures and evident in all human history. Religiosity is a set of traits with great variability among the population. Literature has mainly been focused on the effect of religiosity and spirituality regarding the well-being of the demented patients and their caregivers. Little is known about the neuroanatomical basis of this expression. A small number of studies have correlated religious beliefs and practices with the volume of specific brain regions and particularly right temporal lobe atrophy in patients with frontotemporal dementia. However, the main source of information has been patients with temporal lobe epilepsy that exhibited hyper-religiosity. The aim of present case series that expressed different aspects of religiosity in combination with characteristics in their MRI scans.

Methods: Three dementia patients (2 female, 1 male), age 51-75 years old, two diagnosed with Alzheimer’s disease (AD) and one with frontotemporal dementia (FTD), presenting with cognitive decline of different severity and variable psychiatric symptoms including differences in their religious behaviors, were evaluated. All patients underwent brain magnetic resonance imaging (MRI), with T1, T2 weighted images, T2* and DWI. T1 isotropic images were obtained in two patients and volumetric MRI was performed. Visual evaluation of ischemic lesions, sulcus dilatation and atrophy was performed for all patients, emphasizing on the temporal lobes.

Results: Brain MRI of all patients revealed T2 hyperintensities on the right temporal lobes, due to gliosis and chronic infarcts, although there were not many vascular lesions on the rest of the brain parenchyma (Fazekas 1). Furthermore two patients had severe temporal lobe atrophy and hippocampus volume loss. Sulcal widening and mild volume loss in the precuneus was observed on the third patient.

Conclusions: Three patients with dementia (AD, FTD) presenting with different religious behaviors were evaluated concerning their brain imaging characteristics. In all cases we noted pathology especially in the right temporal lobe, in terms of either gliosis or cerebral atrophy. This region has previously been suggested as a locus for religious activity in the brain and our data further support this idea. Further research is warranted to establish a potential correlation.

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Introduction: Pauses may be studied as an aspect of the temporal organization of speech, as well as an index of internal cognitive processes, like word selection and retrieval, monitoring, articulatory planning, and memory. There are studies demonstrating a specific pattern of pauses in normal speech, however evidence from pathological populations, and especially patients with aphasia is sparse and restricted to small scale studies. The aim of the present study is threefold. First, to investigate possibly different patterns of pause distribution between healthy speakers and aphasics. Second, to examine distinct pause trends among individual patients. Third, to scrutinize possible associations between aphasic pause preferences and lesion characteristics.

Methods: 19 patients with chronic aphasia following a left hemisphere stroke, 40-74 years old, with 6-20 years of formal schooling, were recruited. Structural imaging data (CT or MRI) were obtained for each patient, and lesion sites were identified and coded for 16 predetermined left hemisphere areas: the inferior and middle frontal gyri, the precentral gyrus, the inferior, middle and superior temporal gyri, the inferior parietal lobule, including the angular and supramarginal gyri, the thalamus, the insula, the supplementary motor area, the internal and external/extreme capsule fasciculi, the head and tail of the caudate nucleus, the putamen, and the globus pallidus. The total number of affected cortical and subcortical areas served as an index of lesion extent. The control group consisted of 19 healthy adults, matched for age, gender, and years of formal schooling. All participants were right-handed, native Greek speakers. Aphasic speech samples were derived from recordings of the stroke story interview during standard assessment. Control group participants were asked to provide a brief narration regarding the patient's history. Speech samples were then transcribed, and silent pauses were annotated using ELAN program by two independent raters. All pauses were transformed to log values, using the ln algorithm, while no boundary threshold for pause range was implemented.

Results: Our results indicate that distribution of pauses is bimodal for both groups. That suggests the observed distributions are the result of the combination of two classes of short and long pauses, with medians of 4.85 and 6.51 in the log domain for the non-brain damaged participants and 4.88 and 6.65 for aphasics. Concerning participants with aphasia, different pause profiles are revealed when assessing individual patient data. These profiles seem to be related to indices of lesion extent and locus.

Conclusion: Overall, our findings stress the importance of pauses as an integral part of language assessment in clinical populations, and further support their role in healthy language production as well as impaired speech output. We suggest that pause investigation may be applied to spontaneous speech analysis in communication disorders as well as other quantification measures of speech. Additionally, pauses' locations could be also annotated, in order to specify silence duration before linguistic phenomena.
Introduction: Pure word deafness (PWD) refers to the inability to understand spoken language in absence of any other linguistic disturbance. Patients with PWD are perfectly capable of speaking, writing, and reading; however they present with a striking impairment of auditory comprehension. The etiology of PWD varies, with a vast proportion of cases attributed to cerebrovascular accidents, but there have been reported cases with different neurological diagnoses, such as neurodegeneration or brain tumors.

Clinical Description: We report the case of a 24 year-old woman (EA) with higher education and no prior medical history, who presented with signs of PWD, along with tinnitus and auditory hallucinations. The initial clinical examination revealed phonemic errors during speech, deficits with regard to auditory comprehension, repetition, and writing to dictation. Her speech was otherwise relatively fluent, and naming, spontaneous writing and reading aloud remained intact. There were no symptoms of auditory agnosia or any focal neurological signs. Two consecutive lumbar punctures were performed with acellular cerebrospinal fluid (CSF), protein and glucose level within normal rates, while polymerase chain reaction of CSF confirmed herpes simplex virus type 1. MRI scan (29 days post onset) revealed bilateral diffuse lesions. Upon neuropsychological assessment (43 days post onset), EA’s speech was fluent, with phonemic paraphasias, characterized by conduits d’ approché. Her naming performance revealed a possible impairment with regard to access to lexical/semantic representations. A receptive vocabulary measure was administered in two modalities, aural and written. Even though the patient performed worse than expected in both modalities, the difference between the two scores was striking (with written modality being superior).

Discussion: In sum, this is a case of word deafness without auditory agnosia. Linguistic disturbances following a herpetic brain infection have been previously reported, but the patient’s profile did not fit PWD (Ingles, Mate-Kole, & Connolly, 1996). There is however a case with auditory agnosia that gradually resolved to PWD who report negative laboratory and biopsy culture results, and claim that the macroscopic examination during biopsy revealed focal lesions that “felt to be compatible with encephalitis” (p. 327) and that the patient’s impairment “was presumed to be due to a viral encephalitis” (p. 330) (Goldstein, Brown, & Hollander, 1975).

Conclusion: To our knowledge this paper presents the first confirmed case report of PWD due to herpes simplex encephalitis. Our patient’s neuropsychological profile could be explained in the context of impaired lexical processing, due to lesions affecting association temporal cortices within the perisylvian language network, with the primary auditory cortex and other temporal regions involved in higher-level processing of non-verbal sounds being spared.

References:
**PP29 | Verbal working memory deficits in left and right brain damage**

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**Background:** The established consensus for hemispheric specialization dictates that the processing of verbal information is conveyed by the left hemisphere, while the right hemisphere is dominant for processing visuospatial stimuli. However, there are indications for modality independent deficits due to lateralized lesions (Kasselimis et al., 2013). The present study aims to investigate verbal and visuospatial working memory deficits in left- and right-brain damaged patients.

**Methods:** Fifty (13 women) individuals with chronic aphasia resulting from a left-lateralized cerebrovascular accident (henceforth LBD) and 16 (8 women) right-stroke patients (henceforth RBD) were recruited for this study. Age ranged from 24 to 86 years (Mean: 60.34, SD: 15.54) and from 39 to 76 years (Mean: 57.50, SD: 9.81), for the LBD and RBD group respectively. Years of formal schooling ranged from 4 to 20 (Mean: 10.92, SD: 4.07) and from 6 to 23 (Mean: 12.07, SD: 4.98), for the LBD and RBD group respectively. The two groups were matched for age, gender, and years of formal schooling. It should be noted that aphasic patients with severe fluency and/or comprehension deficits were not included in the study, based on exclusion criteria used in previous studies (Potagas et al., 2011). A digit span task was used as a measure of verbal working memory. The particular test consists of two conditions: forward (the participant is asked to simply retain a series of numbers) and backward (the participant is asked to recite the numbers in reverse order).

**Results:** Product scores (span length*span score) were first calculated separately for forward and backward digit span. A preliminary investigation using the Shapiro-Wilk and Kolmogorov-Smirnov criteria (for RBD and LBD respectively), revealed violations of the normality assumption, thus non-parametric analyses were subsequently implemented. Comparison between mean performances with the M-U test revealed statistically significant differences, with the LBD group being inferior to the RBD group. Further one-sample Wilcoxon Signed Rank Test analyses revealed lower than expected mean performances for both groups on both conditions (the critical value was decided on a normative study by Kessels et al., 2008).

**Conclusion:** Our data indicate that LBD patients are significantly inferior to RBD individuals with regard to verbal working memory capacity. Nevertheless, both groups demonstrate verbal working memory deficits. It could be therefore hypothesized that at least some aspects of online processing of verbal information are affected by bilateral lesions. Issues of lateralization of widely distributed networks supporting verbal working memory in both hemispheres are also discussed.

**References:**
PP30 | A neuropsychological study of mild cognitive impairment as predictor of Alzheimer’s disease

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Introduction: It has been reported that approximately 70% of mild cognitive impairment (MCI) progress to dementia after about three years. The aim of our study is to investigate effective neuropsychological tests to predict the outcome of Alzheimer’s disease in MCI by comparing the results of neuropsychological tests retrospectively between two groups of MCI patients who converted to AD and who did not.

Methods: Twenty-nine (male=15, female=14; mean age; 71.7 (SD=8.6), Clinical Dementia Scale; 0 or 0.5, Mini-Mental State Examination; 27 or more) outpatients were recruited from Memory Clinic at Keio University Hospital. After a mean follow-up of 36.8 (SD=11.4) months, 10 MCI patients progressed to AD (Converter) and 19 MCI patients remained stable (Non-convertor). The two groups were not different in age, sex ratio education attainment, duration of the follow-up examination. They were administered a battery of neuropsychological tests including Raven’s Colored Progressive Matrices, Rey Auditory-Verbal Learning Test (RAVLT), Rey-Osterrieth Complex Figure Test (ROCFT), Logical Memory subtest in Wechsler Memory Scale Revised, Trail Making Test, Stroop test, Verbal Fluency Test at the first medical examination.

Results: An independent t-test revealed that Convertor showed lower scores on the total immediate recall, the difference between the 1st and the 5th trial of immediate recall, and recall after interference on RAVLT, delayed recall on ROCFT, delayed recall on Logical memory subtest than Non-convertor. Moreover, Convertor showed higher score of recency effect on the serial position of the RAVLT and more false positive errors in recognition on RAVLT. However, there was no difference in performance on the frontal lobe functioning tests between the two groups.

Conclusion: Early MCI patients who converted to AD after three years showed a decline in both verbal and visual memory tests. They showed a flat learning curve of immediate recall and the recency effect on the serial position was not impaired on the verbal learning test: RAVLT. Although they made more false positive errors on recognition test, the performance on the frontal lobe functioning tests was spared. The results of our study suggest the effectiveness of memory tests of RAVLT, ROCFT, Logical memory subtest as the predictor of outcome for MCI due to AD.

PP31 | Is executive dysfunctioning an important mediating factor between geriatric depression and suicide?

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Suicidal behavior, either in form of suicidal ideation or in form of attempts appear to be a frequent phenomenon in psychogeriatric populations diagnosed with mood disorder, especially with monopolar depression. A number of studies have proved the positive association between the level of suicidal behavior and the existence of executive dysfunctioning in such populations. Factors such as sex, age and level of education seem to not mediate between neuropsychological profile and suicide intensity; on the other hand, there are remarkable studies results that recognize the onset time and duration of depressive disorder, and existence of common psychological stressors as important mediating factors in this poor cognition and suicide relationship.
Recent reviews have shown cognitive control, described by inhibition ability, executive attention and flexibility to be the highest weakness in neuropsychological profile of this population. Cognitive control is related to person’s ability to allow, review and prevent negative or inappropriate thoughts and emotions from occupying mental resources of working memory. Patients belonging to above populations, perform highly in mental inflexibility, obsession, rumination and mental content dysregulation tests, demonstrating cognitive control deficits.

This particular announcement presents the first data coming from a PhD thesis that takes place in 1st Psychiatric Clinic of Aristotle University of Thessaloniki, regarding the relationship between cognitive control and suicide ideations and behaviors, among other relationships, as these are being examined via a neuropsychological battery for executive functions, inventories and clinical interviews correspondingly, provided to psychogeriatric populations with active depressive symptoms. Furthermore, theoretical frameworks of non-pharmaceutical therapeutic approaches that are being applied to such populations are to be briefly reviewed, so related suggestions to be made.

**PP32 | Planning and problem solving performance in geriatric depression**  
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A very small number of researches have shed some light on problem solving and planning (PSP) performance of geriatric depressed population arguing that older age and negative mood that both affect the cognitive processes that are important for successful performance on related tasks, are impaired. More specifically, PSP abilities are part of the broader term of executive functions that includes planning, execution, monitoring and revising of a purposeful action or a goal-directed behavior. In general, it is well established that executive functions are affected by geriatric depression but it is not clear yet which specific functions are most impaired or which afflict others.

PSP abilities seem to be very important for daily life functioning of older age population, as long as the person is called to adopt new routines, to make decisions about her/his health, etc. Two well-known neuropsychological tasks that assess PSP abilities are the Tower of London and the Tower of Hanoi tasks. Both tests need the engagement of a many cognitive abilities such as attention, spatial working memory, flexibility, inhibition, and of course planning and monitoring. Older adults tend to be slow and not that accurate in both tasks. Also, it is shown that negative mood is correlated to less accurate planning performance, regardless of participant’s age.

This written presentation is going to describe the results arising from a PhD research regarding the executive functions performance in geriatric depressed, non-demented population. For this research we have used an android tablet version of Tower of Hanoi task aiming to evaluate the PSP abilities on an easy and practical way. Additionally, specific data such as time for completion, number of effective or unnecessary moves and strategic thinking information will be analyzed in combination with working memory and attention tasks results.

**PP33 | A case of neurocysticercosis: Neuropsychiatric manifestations**  
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Introduction: Neurocysticercosis is the most common parasitic infection of the human central nervous system. It is endemic in South East Asia, India, China, Latin America and Africa with prevalence rate from 0.4 to 4%. Its prevalence is increasing in Europe mainly due to the influx of immigrants from the endemic areas and due to increasing travels in these countries. Importantly, the long-term course of neuropsychiatric symptoms of patients with neurocysticercosis has not yet been investigated, especially in patients in the calcified stage of the disease and over the age of 60 years.

Clinical Description: We present a rare case of a 68-year-old female patient with bipolar disorder and neurocysticercosis. She was in the chronic calcified stage of the infection. The patient had been diagnosed with cysticercosis since the age of 47 years old when she presented her first manic episode. On admission in our Department she was disoriented, restless, with poor personal hygiene, and manifested flight of ideas, pressured and loud speech (YMRS score: 18, 3MS:89). We treated her with haloperidole 2mg/TID and valproic acid 600mg/day TID (46 mcg/m plasma level). Within one week her manic symptoms remitted, but after one week of normothymia she gradually developed depressive symptoms: sadness, psychomotor retardation, negativism and withdrawal, (total HRSD score was 21). This depression gradually resolved and the patient became normothymic again. Then she has been followed-up monthly for four years treated with monotherapy of olanzapine 210 mg long-acting injection twice a month. Throughout this period she presented cyclical periods of manic-like and depressive-like episodes lasting about one month each with a period of half to one month of normothymia between them. However, her symptoms have been milder with hypomanic symptoms restricted to overactivity and elevated mood and her depressive symptoms characterized only by sadness and withdrawal without catatonic features.

The MRI demonstrated periventricular focal white matter hyperintensities compatible with chronic white matter ischemic changes. The SPECT has shown normal tracer (Tc-99m HMPAO) uptake and brain perfusion. Her cognitive functioning remained stable (3MS initial: 89, final: 84) nevertheless, with constant need of assistance for activities of daily living (IADL initial: 1, final:1). Her neurological examination did not demonstrate any significant abnormalities. Carotid and Vertebral ultrasound gray-scale and Doppler spectral examination showed small non-stenotic plaques in carotid bulb without changes in flow dynamics.

Lastly, there was no interval change in the imaging findings on repeat MRI performed at the end of the follow-up period.

Discussion: Our case underlines the need of close monitoring of patients with neurocysticercosis, especially in middle-aged and elderly patients, as well as the potential effectiveness of long-acting olanzapine in neurocysticercosis with bipolar features.

PP34 | A case report of a suicide prevention intervention for high risk older adults

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Introduction: Suicide is a major public health concern with devastating effects not only on families but on the community as well. Older adults are at high risk for suicide and, older men have the highest suicide rate than any other age group in US [1]. The life events associated with suicide in older adults are those typically following aging: bereavement, financial stressors related to retirement, family discord and loss of
social support, as well as social and psychological impacts of physical illness. The proportion of completed suicides among suicide attempters is also higher in older adults than in the general population, i.e. 1 out of 4 in older adults compared to 1 out of 12 in general population. Recent hospitalization for a suicide attempt is a high risk factor for suicide, especially during the first few months after discharge [2]. Despite the need for suicide prevention interventions for hospitalized older adults, psychosocial interventions for this group are underdeveloped [3]. The current case report describes Problem Adaptation Therapy for Suicide Prevention (PATH-SP), a suicide prevention intervention for older adults who have been recently hospitalized for suicidal ideation or suicide attempt.

Clinical Description: Mr. A. is a 67 years old male who has a history of Major Depressive Disorder, recurrent, severe without psychotic features with age at onset at 60 years old. He was hospitalized for a suicide attempt during the current episode, which was his second. He was admitted in the inpatient Unit of Division of Geriatric Psychiatry of Eginition Hospital after a serious suicide attempt. He was initially treated with antidepressant medication with no response and then he was treated with electroconvulsive therapy with partial response. After being discharged from the hospital, he still had depression symptoms, including sadness, guilt, hopelessness, and worthlessness; Mr. A developed suicidal ideation within a couple of weeks after discharge. He was referred for psychotherapy, i.e. Problem Adaptation Therapy for Suicide Prevention (PATH-SP), which is characterized by a simplified problem solving approach and emotion regulation strategies. Mr. A had great response to this type of psychotherapy.

Discussion: PATH-SP focused on: a) identifying situations that triggered negative emotions and contributed to his suicide attempt and increased suicidal ideation after the hospital discharge and b) developing a plan to reduce these negative emotions and reduce the suicide risk. The selection of this kind of psychotherapy depends on the patient's clinical state, as well as on the acute and chronic stressors, the patient's interpersonal context, skills and behavioral deficits. During the psychotherapeutic sessions, these parameters need to be often reassessed, in order to redefine and successfully treat each patient’s specific needs.

Conclusion: This case report demonstrates the novel use of a combination of a problem solving approach and emotion regulation strategies as an adjunctive therapy to medication treatment for depression and suicidal ideation in older adults at high risk for suicide.

References:

PP35 | Traumatic brain injury in individuals 65 and older: Differences between young and old in head injury characteristics and one-month outcomes

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Introduction: The occurrence of traumatic brain injury (TBI) can best be described as tri-modal with clustering of TBI incidence in very young children, older adolescents, and the elderly. The emergency department (ED) is the most common point of TBI evaluation with an estimated 4.8 million ED patients evaluated for TBI each year. There is a paucity of research focusing on TBI outcome by age. The American College of Emergency Physician (ACEP) criteria for obtaining head computerized tomography (CT) in the setting of suspected TBI includes older age as a criterion. Given this, we hypothesized that fewer individuals in our older age group (>65 years) would meet American Congress of Rehabilitation Medicine (ACRM) criteria for TBI and therefore when examining ED patients evaluated for TBI with a head CT, the older participants would have better one-month outcomes than younger participants. However, when restricting the study population to just those meeting ACRM criteria for TBI, we hypothesized that the older participants would have worse outcomes than younger participants.

Methods: The Head Injury Serum Markers for Assessing Response to Trauma study (HeadSMART) is an ongoing, prospective cohort study examining the utility of blood-based biomarkers in diagnosis of TBI, while also collecting data on cognitive and other neuropsychiatric symptoms longitudinally to analyze the prognostic utility of these biomarkers. In this secondary analysis, we examine differences in demographics, head injury characteristics, and one-month outcomes in older (age >65 years) vs. younger (age <65) suspected TBI participants. Scales used to examine outcomes are: Glasgow Outcome Scale Extended (GOSE), Rivermead Post Concussion Symptoms Questionnaire (RPQ) total score, and Patient Health Questionnaire-9 (PHQ9) score of ≥10 (indicating moderate/severe depressive symptomatology).

Results: The most common mechanism of injury was motor vehicle collision (33.8%) in younger and falls (71.3%) in older. The younger group had more individuals meeting ACRM criteria for TBI (77.8% vs. 64.8%, p<0.01) and higher baseline total RPQ scores (12 vs. 6, p<0.01). Among those meeting ACRM criteria, older individuals were less likely to have a normal head CT (54.3% vs. 76.6%, p<0.01) and more likely to be classified as having a moderate, rather than mild, TBI (45.7% vs. 22.4%, p<0.01). Within the entire study population, and restraining to those meeting ACRM criteria, the older group had better one-month outcomes on all three measures. Among those meeting ACRM criteria, older individuals were more likely to have upper/lower good recovery on the GOSE (75% vs. 61.6%, p<0.01), lower total RPQ scores (5 vs. 10, p<0.01), and were less likely to have moderate/severe depressive symptomatology (27.5% vs. 45.3%, p<0.01) at one month.

Conclusion: We found support for our hypothesis that in all participants evaluated for TBI with a head CT, older individuals would have better one-month outcomes. However, contrary to our hypothesis, among those who met the ACRM criteria for TBI, older individuals continued to have better recovery at one month. This study highlights the importance of studying TBI in the elderly to further understand the differences in TBI outcome between the young and old.

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PP36 | Brain white matter atlas-based analysis in late-life depression: A pilot study

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Introduction: Brain diffusion tensor imaging (DTI) studies in late-life depression (LLD) have focused on the voxel-wise analysis of diffusion contrasts (e.g., Tract-based Spatial Statistics, Voxel-based Analyses,
The aim of the present study was to extend the analysis of brain white matter to a labeled tract group level in patients with LLD.

Methods:
Subjects: Eleven right-handed male (7 acute LLD medicated inpatients, 4 healthy controls - NC) provided written consent in an ongoing case-control study approved by the University of Athens Ethics Committee. Inclusion criteria were age ≥ 55 years, a DSM-IV diagnosis for major depressive episode, and MMSE ≥ 28. Exclusion criteria were a history of neurological/psychiatric disorder (except depression), drug abuse, malignancy, and presence of confluent brain white matter hyperintensities on FLAIR images. The 30-item Geriatric Depression Rating scale was used to rate depression.

Imaging: Non-cardiac-gated diffusion-weighted imaging datasets were acquired in a 3 Tesla, 8-channel coil whole-body MRI scanner (Phillips Achieva TX, Best, The Netherlands) using a single-shot, EPI sequence, with SENSE parallel imaging (reduction factor 2.5). Imaging parameters: bmin = 0 s/mm² (b0), bmax = 700 s/mm², 32 diffusion coding directions, 2.2 mm isotropic voxel size, 70 gapless axial slices parallel to the anterior commissure/posterior commissure line, image matrix 96x96 zero-filled to 256x256, and FOV 212x212mm. DTI was repeated twice to improve the signal-to-noise ratio. Image processing and Atlas-based analysis was performed using the MRI-studio software [1] which calculates the tensor using multivariate linear fitting. Volume fractional anisotropy (FA) (i.e., the number of voxels surviving a published FA threshold of 0.25) as a marker of white matter presence was measured within the predefined white matter parcellation map (80% white matter probability) of JHU-DTI-MNI – “Eve” atlas (http://cmrm.med.jhmi.edu/), after performing linear [2] and non-linear [3] transformations (tri-linear interpolation) of the subject’s FA maps to the atlas coordinates. Non-parametric statistical analysis (Mann-Whitney U) was used to compare the groups’ variables.

Results: Compared to NC, LLD subjects demonstrated statistically significant white matter volume FA reductions in various brain regions. Corona radiata (CR) demonstrated bilateral reductions in patients with LLD compared to NC (right anterior CR, p=0.024; right superior CR, p=0.006; left superior CR, p=0.042; left posterior CR, p=0.012). Further, a significant difference in the association of white matter volume FA reductions and depression was found for the left anterior CR compared to right anterior CR ( p=0.018).

Conclusion: Our preliminary findings of white matter integrity alterations in projection fibers in LLD patients are supported by previous studies. Given the study shortcomings it seems that bilateral reduction in CR volume FA in male patients with LLD may be an important finding. Furthermore, LLD patients indicated a more significant disruption in white matter integrity in left anterior CR volume FA.

References:

PP37 | Old age psychiatry clinic in University General Hospital of Alexandroupolis the first five years of experience
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Aim: This study aims to evaluate the work that was performed in the Old Age Psychiatric Clinic in General Hospital of Alexandroupolis that completed five years of existence since its establishment in 2010.
Methods: We used Hospital records to assess the diagnosis that were given to the patients to calculate the annual number of visits in the clinic during the last five years as well as visits frequency. We also analyzed the scores of the psychometric tests that were used, GDS, Mini Mental test, Clock Test, Verbal fluency, in order to draw some conclusions regarding the effect of our approach. Lastly we analyzed the medication that was administered to the patients.

Results: More than 200 patients were served in the clinic during its first five years. There was a significant increase more than 60% of annual visits from its first year of operation in 2010 until 2015. Most of cases regarded depressed patients. There was a significant improvement in GDS as an average. Cognitive functioning as it was assessed by the bedside psychometric tests was stable in most of the cases. Frequency of the visits was around 2 per year but the great majority of the patients had a stable follow up in the primary care. Patients were taking from 1 to 6 different medications with an average of more than two when they first visited the clinic, medication was decreasing during the follow up. A special reference is also made in the educational part of the Clinic. More than 15 trainees in Department of Psychiatry, psychiatry trainees, neurology trainees, general practitioner trainees and psychologists and some medical students assisted the clinic. Most of them either gained a useful experience or they were motivated enough to continue to work in Old Age Psychiatry field. Training wise also the psychometry that was used, made it possible for our department to conform in a great extend with General Practitioners' log book requirements for their training in psychiatry, since these requirements are for GP trainees to complete a number of GDS and Mini Mental Tests.

Conclusions: Old Age Psychiatry Clinic in General Hospital of Alexandroupolis has established its existence during the last five years. It has a significant role in the area, as it is apparent from the constant increase of the patients that attend the clinic. Patients improve regarding their disease load as well as their medication load, these can be considered as positive results of our practice. The introduction of psychometry in clinic practice was also something novel and it is now followed by other colleagues in the Psychiatry Department. Training opportunities were increased for doctor trainees as well as other scientists in the department. We can say that we are satisfied from our first five years. Our next steps for the future aims mainly to our connection with other much more advanced Old Age Psychiatric Clinics in Greece and the use of common data bases in order to facilitate research the lack of which is our main weakness.

PP38 | Psychological effects on caregivers of a dementia-specific hospitalization clinic

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Introduction: Dementia caregiving burdens the physical, psychological and socio-economic status of those providing care, more than the caregiving for patients with other chronic diseases [1]. Researches indicate that a high percentage of dementia caregivers suffer from depression and anxiety, while they report poor quality of life and more physical and psychological symptoms than non-caregivers [2,3]. In effect, various interventions have been developed these past years in order to decrease the burden for dementia caregivers and improve the quality of care provision for dementia patients. Nestor Psychogeriatric Association, aiming to alleviate the burden of dementia caregivers in Athens, Greece,
established a Short-term, 15 bed, Hospitalization Clinic, since 2004. Services are free of charge and the hospitalization is for maximum one month time.

**Methods:** The purpose of the specific study was to examine the psychological effects of the dementia patients’ brief hospitalization on their caregivers. Burden of caregiving (Zarit Burden Interview, ZBI), depression (Center for Epidemiologic Studies Depression Scale, CES-D) and stress (Kingston Caregiver Stress Scale” (KCSS) were evaluated before and after hospitalization in order to determine its effects on caregivers’ psychological status. The results that were collected were analyzed with the statistical packet SPSS 22.0. Our sample consisted of all 36 dementia patients who received the service of brief hospitalization during one year time (January 2015-December 2015) and their family caregivers.

**Results:** Patients had a mean age of 82.3 years old, most were women (n=22, 61.1%) and suffered from severe dementia (mean Mini Mental State Examination score 6.4). Out of the 36 caregivers, 26 were women (72.2%) with a mean age of 58.2 years old. 92% caregivers lived with the patients and only 16.7% had a professional caregiver. The majority of the caregivers participants were women, and more specifically 47.2% of them were daughters. After evaluating the questionnaires, prior to the hospitalization, caregivers showed burden (ZBI) with a mean of 48.3, while in the second evaluation burden decreased to 46.6 (p=0.79). Mean CES-D value was 20.9, while after the period of patient hospitalization decreased to 18.4 (p=0.15). Interestingly, CES-D score significantly decreased in women after hospitalization (p=0.03). KCSS mean also decreased from 34.2 to 32.6 (p=0.38).

**Conclusion:** Our short term hospitalization clinic is one of the very few, if not the only. The results of the current study show that hospitalization decreased all three indicators of caregivers’ psychological status (burden, depression and stress), although not in a statistically significant level. Small sample size of our study may play a role. Women and men may experience burden in a different manner and benefit from interventions may vary according to gender differences. Further studies are needed since relevant research is very limited.

**References:**

**PP39 | Effectiveness of multi-domain cognitive intervention groups on a sample of normal and mild cognitive impairment individuals**

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**Introduction:** As dementia prevalence increase, finding efficient non-pharmacological treatments for those with subjective memory complains and mild cognitive impairment (MCI) is important. Recently, cognitive interventions gained popularity and studies revealed that they may be effective in enhancing...
specific cognitive capacities. Nestor Psychogeriatric Association implemented cognitive intervention groups of 8-10 persons, grouped according to their cognitive function level.

Methods: The purpose of the specific study was to examine the impact of the cognitive intervention groups on specific cognitive functions to both normal subjects and those with MCI. The Mini Mental State Examination (MMSE), the Rey’s Auditory Verbal Learning test, clock drawing test (CDT), One-minute Semantic Verbal Fluency (SVF) test for the category “animals” and one-minute Phonemic Verbal Fluency (PVF) for words starting from three different Greek letters were used. Data were recollected after six months of intervention and analyzed with the SPSS 22.0. Our sample consisted of 56 subjects, 24 (42.9%) cognitively normal and 32 (57.1%) with MCI (treated in seven groups of eight persons each).

Results: Participants were mostly women (n=49, 87.5%), with a mean age of 70 years old and 12 years of education on average. The two groups did not differ significantly in terms of age and education. The MCI group showed statistically significant improvement in Rey’s first and second immediate recall, late recall and Semantic Verbal Fluency (SVF) test for the category “animals”, whereas the group of normal individuals solely showed significant improvement in Rey’s recognition.

Conclusion: Our research findings are in line with previous researches indicating that cognitive interventions may produce improvement in specific measures of cognition functioning such as immediate or late recall and verbal fluency. Further research is needed to indicate if cognitive interventions may delay dementia progression or improve functioning. As a specific Alzheimer’s plan is about to be launched in Greece, the present study underlines the importance of implementing cognitive intervention groups targeting both individuals with subjective memory complains and MCI in the Greek population.

References:

PP40 | A systematic review of pharmacological and non-pharmacological treatment of apathy in Alzheimer's disease
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Objective: Apathy is one of the most frequent neuropsychiatric symptoms encountered in Alzheimer’s disease (AD). Early diagnosis and timely treatment of apathy in AD seems to be of great importance since apathy has been associated with poor disease outcome, reduced daily functioning and caregiver distress.

Design: Within this context we conducted an extensive electronic search from the databases included in the National Library of Medicine as well as PsychInfo and Google Scholar for studies which have investigated the effect of pharmacological and non-pharmacological treatments of apathy in AD.

Results: Acetylcholinesterase inhibitors, gingko biloba, methylphenidate and a variety of non-pharmacological interventions were found to be successful in reducing apathy in patients with AD.
Methodological heterogeneity of the studies and the small amount of studies where apathy was a primary outcome measure are limiting factors to evaluate for group effects.

Conclusions: Treatment of Alzheimer’s disease apathy is a complicated and underexplored field. Standardized and systematic efforts primarily focused on the study of Alzheimer’s disease apathy may establish a benefit from individualized treatment for specific disease groups that would stem from a combination of both pharmacological and non-pharmacological interventions.

PP41 | Heart rate variability predicts treatment outcome in major depression and may predict treatment outcome in bipolar depression

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Introduction: Autonomic nervous system (ANS) dysregulation in bipolar disorder can be measured in a variety of clinical presentations and symptoms. The beat-to-beat pattern of heart rate, “Heart Rate Variability”, abbreviated as HRV, provides a noninvasive measure of ANS function. HRV quantifies the periodic heart rate pattern during the frequency of spontaneous breathing known as Respiratory Sinus Arrhythmia (RSA), which is synonymous with high frequency HRV (HF-HRV). We quantified RSA, low frequency HRV (LF-HRV), and heart period (HP) in treatment resistant bipolar depressed patients in order to indirectly measure possible ANS dysregulation. We sought to determine whether RSA, LF-HRV, and/or HP are potential diagnostic markers and/or potential predictors for treatment response.

Methods: This was a double blind placebo controlled randomized trial aimed at ascertaining whether modulation of the inflammatory response by means of Celecoxib (COX-2 inhibitor) will lead to reversal of treatment resistance and augmentation of treatment response. In one arm of the study, patients received Escitalopram (ESC) + Placebo, in the other arm, patients received Escitalopram (ESC) + Celecoxib (CBX). Patients were treated for 8 weeks and assessed at specified intervals. CBX was added to one arm of the treatment group to determine if a non-steroidal anti-inflammatory drug could be used in conjunction with a traditional SSRI to augment treatment response. Forty-seven patients completed the study. RSA, LF-HRV, and HP were assessed at baseline (pretreatment) and end of treatment and compared with that of healthy control subjects at baseline. RSA was quantified and corrected for respiratory and other artifacts using an algorithm that incorporates both time and frequency domains to address the inherent nonstationarity of the beat-to-beat heart rate pattern (Cardiobatch).

Results: Both the ESC group (p=0.072) and the ESC + CBX (p=0.048) groups extended HP at the end of the 8-week study. Previous research on Major Depressive Disorder (MDD) from our laboratory (Hage et al., under review) has shown that a high baseline HRV is a predictor of treatment response. In the present study, we did not find statistically significant differences in baseline RSA between responders and non-responders regardless of treatment group. However, raw HRV values did suggest a trend that higher HRV could lead to a greater likelihood of treatment response in the ESC + CBX group. We believe that statistical significance could be possible if the groups were larger. Also, the possible effects of antidepressants and mood stabilizers the patients were receiving might have exerted independent effects on HRV.

Conclusions: ESC and ESC + CBX extend HP significantly, indicating strengthening of vagal tone and thereby enhancing probability of future remission. We propose that either treatment, if successful, may lead to a strengthened vagal tone in bipolar depressed patients. Further research is needed to confirm the present findings with ESC and HP and to investigate whether other antidepressant drug treatments...
produce similar effects. The question remains whether mood improvement per se, independent of treatment modality utilized, is the critical factor responsible for the extension of HP and enhancement of vagal tone.

PP42 | Assessing peripheral biomarkers during cyclooxygenase-2 inhibitor combination treatment for bipolar depression

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Introduction: Chronic immune system activation has been closely associated with depression with elevated pro-inflammatory biomarkers including C-reactive protein (CRP) and interleukin-6 (IL-6). Mounting evidence also links decreases in vascular endothelial growth factor (VEGF), a neurotrophin, to depression. Chronic subthreshold pro-inflammatory status may interfere with an antidepressant’s ability to exert its therapeutic action. In this randomized, double-blind study, poorly responding bipolar patients were treated with the SSRI, escitalopram (ESC). One group received the cyclooxygenase-2 (COX-2) inhibitor celecoxib (CBX), and the other placebo. COX-2 inhibitors were selected because they reduce inflammation by blocking synthesis of prostanoids. We hypothesized that both groups would initially show decreased VEGF and elevated CRP/IL-6 compared to healthy controls, and that treatment with CBX would increase VEGF and decrease CRP/IL-6 levels more than placebo.

Methods: Patient plasma was obtained at baseline, weeks 4 and 8. CRP concentrations were measured by enzyme-linked immunosorbent assay (ELISA) using the Aniara Zymutest by HYPHEN Biomed®. VEGF and IL-6 concentrations were obtained via Randox® Biochip Array. VEGF concentrations were also obtained via ELISA using the R&D Systems® kit. Statistical analyses were conducted using Prism by GraphPad Software®.

Results: CRP levels were significantly increased in patients compared to healthy controls at baseline (P=0.044; analyzed with Mann-Whitney test, MWT). The CBX treatment group showed insignificant CRP differences at baseline compared to placebo (P=0.156), yet CRP was significantly decreased in the treatment group versus placebo by week 8 (P=0.003). VEGF levels were significantly elevated in patients vs. healthy controls at baseline (P=0.021). By week 8, VEGF remained elevated in all patients vs. healthy controls (P=0.007), and there were no significant differences in treatment vs. placebo VEGF at week 8. IL-6 showed elevated mean concentrations in patients versus healthy controls at all time points, but no significant differences were seen. A positive Spearman correlation was seen between CRP and IL-6 in the treatment group at baseline (P=0.045, R=0.404) and also between VEGF and IL-6 in the treatment group at week 8 and placebo group at baseline (P=0.001, R=0.661; P=0.04, R=0.53). No significant correlations were seen between CRP and VEGF. Positive correlations were seen between the VEGF ELISA vs. VEGF Randox, with P values <0.05.

Conclusions: The elevated baseline CRP and decreased baseline VEGF in bipolar patients was consistent with our hypothesis. Therefore, CRP and VEGF may be biomarkers for bipolar depression. When treated with CBX, CRP decreased significantly compared to the placebo group, indicating that inflammation is significantly reduced in CBX-treated patients and very likely responsible for the enhanced treatment outcome we observed. Furthermore, CRP testing can possibly be used to assess efficacy of COX-2 inhibition during combination treatment. Peripheral VEGF seems to be unaffected by COX-2 inhibition, as no increase was seen in VEGF in patients treated with CBX compared to placebo. Correlations were seen between IL-6 and CRP as well as IL-6 and VEGF, but not between VEGF and
CRP. The positive correlation between the VEGF ELISA and Randox indicated good inter-assay reliability between two diverse assay methods.

**PP43 | Arterial stiffness as an index of inflammation in patients with bipolar depression**

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**Introduction:** Arterial stiffness has been correlated with increased risk of stroke, heart disease, and death over a 10 to 12-year period. Aging, hypertension, and dyslipidemia contribute to the stiffening of the arterial wall. Additionally, inflammation is associated with endothelial dysfunction and arterial stiffness beyond the expected stiffening due to natural aging processes and other cardiovascular risk factors. Psychiatric illnesses, including bipolar disorder (BPD), have been associated with a pro-inflammatory state and thus assessment of arterial stiffness may be an important factor in overall diagnosis and treatment. Non-invasive techniques, such as applanation tonometry (AT), are useful in evaluating arterial stiffness by reflecting intra-arterial pressure. Pulse wave velocity and Augmentation Index (AIx) serve as indicators of elasticity or rigidity of the arterial wall. We measured AIx in patients with BPD and healthy controls, to establish a potential link between inflammation and cardiovascular risk. Due to the established link between depressive illness, inflammation, cardiovascular risk and overall anti-depressant drug response, we designed a study with the COX-2 inhibitor Celecoxib (CBX) to modulate immune response.

**Methods:** Forty-seven treatment resistant BPD patients were enrolled in a double blind study design and received Escitalopram (ESC) + CBX or ESC + Placebo over an eight-week treatment period. AIx was measured at baseline and end of treatment. Twenty-seven patients with complete data sets were included in the present analyses. Thirty-nine healthy subjects served as controls. Comparisons of AIx were conducted between BPD and healthy subjects at baseline, between treatment groups, and between baseline and end of treatment in all BPD subjects.

**Results:** We examined age, BMI, MAP, total cholesterol, LDL, HDL, triglycerides, tobacco use, and menopausal status as possible confounding variables in all study subjects. Both female and male BPD patients had a higher AIx than their healthy control counterparts, but when controlling for the confounding variables, no statistically significant difference emerged. Amongst the confounding variables assessed, age consistently emerged as a significant variable in both sexes, but more so in males. When age effect was further analyzed by subgrouping into <39 and ≥39 years of age, the effect of depression as a key contributory factor in AIx was unmasked in the younger age group. Amongst lipids, triglycerides were a significant confounding factor (p=0.017) in males. AIx in the ESC+ Placebo group trended toward decrease at the end of treatment (p<0.076). No correlation was determined between severity of depression and anxiety, as assessed by HAM-D 17, HAM-D 21, HAM-A or MADRS and AIx at baseline.

**Conclusions:** We propose that AIx, as a marker of arterial stiffness, cannot be independently attributed to inflammation in bipolar depression. Our study has confirmed age as a significant variable in arterial stiffness measured by AIx. In subjects under 39, the contributory effect of age on arterial stiffness is minimized, thereby allowing the effect of depression to be unmasked. Assessment of augmentation index among young BPD patients may be an important area of focus, highlighting the potential utility of AT in overall treatment and intervention.
The role of inflammatory biomarkers and neurotrophins in bipolar disorder

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Introduction: It is generally accepted that the immune system plays a key role in the pathophysiology of mood disorders. Many patients diagnosed with major depressive disorder (MDD) have increased levels of IL1, IL6, IL8, IL1β, TNF, and CRP consistent with immune system activation and stress related disorders. A chronic pro-inflammatory state has been associated with poor response to antidepressant medication. Pro-inflammatory mediators can interfere with serotonergic transmission, leading to reduced post-synaptic availability of serotonin. This paper focuses on inflammatory and neurotrophic biomarkers in patients diagnosed with bipolar depression (BPD).

Methods: This double-blind, placebo-controlled study was designed to investigate the potential benefit of inflammation modulation by combining a standard SSRI, escitalopram (ESC) with a COX-II inhibitor, celecoxib (CBX). Over 8 weeks, bipolar patients with treatment-resistant depression were given ESC+Placebo or ESC+CBX. We hypothesized that those receiving the combination treatment would show an augmented and more rapid response to ESC. We analyzed inflammatory and neurotrophic biomarkers. We examined the possible relationship between these biomarkers and treatment outcomes. Healthy control subjects (N=38) were used for comparison purposes. The severity of depression was assessed by the HAMD-7, HAMD-17, and HAMD-21 rating scales.

Results: Bipolar patients had significantly higher proinflammatory biomarkers (IL2, IL4, IL8, TNFa, and IL1β) at baseline and week 8 when compared to healthy controls. Both treatment groups examined together trended toward a decrease in IL2, IL4, IL6, IL8, and TNFa by week 8. When separating the two treatment groups and comparing % change in cytokine levels between baseline and week 8, the only cytokine that differed markedly was IL1β. Those patients who received ESC+CBX showed a decrease in IL1β over the 8 week time period that trended toward significance. The ESC+Placebo cohort did not. Depression severity decreased at week 8 in both groups. CBX+ESC patients had a significantly augmented and earlier response to treatment determined by the HAMD scales. The neurotrophic factor, VEGF, was significantly higher in the bipolar cohort compared to healthy controls. VEGF levels did not change in either treatment group during the study. Lastly, we correlated the inflammatory biomarkers with VEGF across treatment groups and healthy controls. Of note, IL10, a robust anti-inflammatory cytokine, was positively correlated with VEGF in healthy controls. In bipolar patients, VEGF and IL10 were not correlated before treatment. However, at week 8, the patients on combination treatment had plasma IL10 levels that correlated significantly with VEGF. The ESC+Placebo treated patients did not.

Conclusions: IL1β is a pro-inflammatory cytokine that decreases the bioavailability of serotonin. The decrease in IL1β in patients receiving combination treatment may be associated with enhanced therapeutic response. The increase in VEGF might be a neuronal attempt to compensate for the chronic pro-inflammatory state. Lastly, we propose celecoxib is working to increase the anti-inflammatory state through an increase in IL10 and other mechanisms, contributing to the improved treatment outcomes. Future studies are necessary to flesh out the psychoneuroimmunological complexities to effectively use immunological biomarkers to personalize psychiatric care.
POSTER PRESENTATIONS SESSION 2
Psychiatry

PP45 | In search of an integrated profile of the Greek gambler: A preliminary, multidisciplinary approach
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Introduction: Pathological Gambling (PG) is a disorder characterized by a persisted maladaptive and recurrent behavior with severe social and psychological effects. Evidence-based research indicates high rates of comorbidity with several aspects of psychopathology. Neuropsychological deficits have been also reported, mainly related to executive functions like inhibition, planning, shifting, and cognitive flexibility. Regarding personality traits, PG has been associated with high rates of impulsivity while sensation seeking seems to be a common characteristic among gamblers. However the majority of the relevant literature derives from treatment seeking gamblers, a non representative share of the global PG population. Our study aimed to investigate anxiety and depression signs, possible cognitive impairment in executive functions and working memory, and personality traits in a non-treatment seeking Greek PG sample.

Methods: Twenty four males, 30-68 years old (Mean: 45.5; SD: 10.6) with 6-23 years of formal education (Mean: 14.58; SD: 4.17), with mixed gambling activity were recruited from ecological settings and identified with SOGS as problematic and probably pathological gamblers. They were assessed with a neuropsychological battery, the Zuckerman-Kuhlman Personality Questionnaire, the Hospital Anxiety Depression Scale, and the Difficulties in Emotion Regulation Scale. Their performance was compared to scores derived from 21 non-PG males. There were no differences with regard to mean age and years of formal schooling between the two groups.

Results: Analyses revealed significant differences between gamblers and controls with regard to neuropsychological measures related to inhibition and decision making, personality factors related to impulsivity/sensation seeking and emotional awareness (with the PG group being inferior). Notably, gamblers demonstrated significantly higher performance on measures of working memory, processing speed and verbal fluency. Results with regard to anxiety and depression indices failed to reach significance.

Conclusion: Overall, our study highlights cognitive, personality, and possible psychopathological aspects of Greek gamblers. The main components of the gambler’s profile seem to be impaired inhibition, problematic decision making strategies, increased impulsivity, and low emotional awareness, without however prominent signs of anxiety or depression. Qualitative data from a semi-structured interview integrate the aforementioned profile. The observed superiority of gamblers on particular measures of working memory and executive functions could be interpreted in the context of gradual development of strategies through their chronic gambling activity. Issues concerning psychopathological co-morbidities, as well as the alleged gambling-related “dysexecutive syndrome” are also discussed.
**PP46 | Burnout in the Intensive Care Unit professionals**

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**Introduction:** Burnout syndrome has been described as an inability to cope with emotional stress at work. Burnout Syndrome is defined as a condition of mental suffering work-related and associated with physiological changes resulting from stress. The burnout syndrome is experienced mainly by health professionals involved in care activities, where the greatest demand for this type of service is to deal with the emotional needs of the other, under stress. Nurses and physicians working in the intensive care unit (ICU) may be exposed to considerable job stress. The aims of this study were: (1) to investigate burnout syndrome among health professionals working in intensive care units, (2) to determine the causes and the consequences of burnout syndrome, as well as the clinical implications of burnout in the intensive care unit, the solutions and the preventive measures in order to cope with burnout syndrome and (3) to investigate the relationship between the development of burnout in the staff of ICU and traits of personality, as well as sociodemographic and professional characteristics.

**Methods:** A literature review was conducted in Medline and Scopus database regarding the above parameters of burnout syndrome. The keywords used in the literature search were “burnout”, “Intensive Care Unit” and “Intensive Care Unit professionals”.

**Results:** Burnout syndrome incorporates the physical as well as the mental exhaustion observed in every professional whose work needs continuous contact with other people. The syndrome does not emerge suddenly. It is the product of a long time of stressful working. Because of the nature of this highly specialized form of nursing, ICU professionals can experience high levels of psychologic and physical stress and, therefore, high levels of severe burnout syndrome. Difficult decisions about end-of-life care are made, and burnout is found to be frequent among ICU staff. Burnout is a response to workplace stress that results in emotional and mental exhaustion, depersonalization and decreased sense of personal accomplishment. The effects of health professional burnout and stress in an Intensive Care Unit can have detrimental effects on health care. The above results underscore burnout syndrome as a significant and ubiquitous challenge that needs to be openly embraced and actively managed. Job satisfaction, emotional support, and self-care are important components for preventing burnout in staff.

**Conclusion:** The ICU is a highly stressful environment, not only for patients and relatives but also the staff. The burnout syndrome is present in health-care professionals in ICU. We must be aware of this phenomenon in order to study it and to reduce it. It is the responsibility of both individual health professionals and hospital administrative leaders to take the necessary interventions to prevent work stress and burnout.

**PP47 | Depression, anxiety and psychological distress among parents of infants admitted to a Neonatal Intensive Care Unit**

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**Introduction:** Parents of infants admitted to a neonatal intensive care unit (NICU) experience heightened distress, significant symptoms of depression and anxiety disorders because they are rarely prepared for the shock, stress and anxiety when their infant is sick enough to require critical care in a NICU.
Methods: A literature review was conducted in Medline and Scopus database regarding the above parameters of burnout syndrome. The key words used in the literature search were “Depression”, “Anxiety”, “Psychological Distress”, “parents”, “hospitalized infants”, “neonatal intensive care unit”.

Results: Besides the normal stress of parenthood, parental distress has been related to different factors, including physical and emotional isolation from the baby, a sense of lack of control, the need of adapting to having a sick infant, the stress of the NICU environment, the need for timely medical information presented in an understandable language as well as additional stressors when parents live too far away from the hospital. The environment, technology, appearance of the infant and the feeling of a loss of the parental role contribute greatly to the amount of stress found among parents in the NICU. The appearance and behavior of a sick infant, the use of complex medical language and technology, threat of potential loss of their child’s life, and parents’ loss of their role in their infant’s care are a few of the stressors which can compound existing parental distress about their infant’s illness. In these circumstances parents have reported a variety of reactions, including sadness, fear, anxiety, grief, and helplessness.

Conclusion: The prevalence of poor psychological well-being among parents of infants admitted to a neonatal intensive care unit highlights a critical role for NICU providers as neonatal care providers have a unique relationship with parents and a golden opportunity to identify symptoms and provide appropriate referrals and support.

PP48 | Suicidal behavior in adolescents and children
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Introduction: Suicide can occur at any age and is a significant public health concern. Suicidal ideation and attempted suicide are frequent presenting problems in both adult and child psychiatric facilities. The aim of this study was to examine the descriptive epidemiology, as well as the risk and protective factors for youth suicide and suicidal behavior in children and adolescents, involving mental and physical disorder, personality and psychological traits, family factors, biology, developmental stage, access to lethal agents or methods used.

Methods: A literature review was conducted in Medline and Scopus database regarding the above issues. The keywords used in the literature search were “suicide”, “children”, “adolescents”, “suicide attempts”, “suicide prevention”, “suicidal ideation”, “suicidal behavior”, “risk factors”.

Results: The magnitude of this public health problem and the morbidity and mortality that results from the feeling that life is not worth living have stimulated a sizable and growing body of research. The rate of completed suicide and attempted suicide in young people increases our need to understand the antecedents of suicide and the relationship among suicidal ideation, suicide attempts, and completed suicide. Suicidal behavior ensues as a result of an interaction of socio-cultural, developmental, psychiatric, psychological, and family environmental factors. What is known about the epidemiology, causes, risk factors, management, and prevention of suicide and attempted suicide in young people may lead to detailed guidelines concerning the assessment and emergency management of the children and adolescents who present with suicidal behavior and may also present suggestions on educational programs, screening/case-finding suicide prevention strategies and the training of primary care professionals and other gatekeepers to recognize and refer the potentially suicidal child and adolescent.

Conclusion: Progress has been made in our understanding of the phenomenology and risk factors of adolescent and child suicide and suicidal behavior. The roles of caregivers and schools are more salient in the assessment, management, and prevention of suicidal behavior in children and adolescents. On the
basis of this review, clinical and public health approaches to the reduction in youth suicide and recommendations for further research are discussed.

**PP49 | A case series of patients with schizoaffective disorder in a Mood Disorder Unit**

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**Introduction:** The diagnosis of schizoaffective disorder is frequently used to describe the co-occurrence of both schizophrenic and affective symptoms, but the conceptualization and nosological status of this disorder remain contentious [1]. The inter-clinician reliability of a diagnosis of schizoaffective disorder has been reported to range between poor and moderate [2]. The temporal stability of the schizoaffective disorder diagnosis is relatively low [3]. In this study, we aimed to describe the clinical characteristics obtained from medical records and tried to exam to what extent the daily use of the schizoaffective disorder diagnosis was in accordance with the DSM-IV-TR criteria.

**Methods:** We presented all three patients who were diagnosed with schizoaffective disorder and were admitted in a specialist Mood Disorder Unit in the Institute of Mental Health from 1 May 2012 to 31 March 2015. The Institute of Mental Health is the only tertiary psychiatric hospital in Singapore with 2,000 inpatient beds, which serves a local population of 5.5 million people. The cases of the three patients who enrolled in this study were described in detail with regard to demographics and psychiatric history. We obtained all the information from our medical records. This study was approved by the Clinical Research Committee of the Institute of Mental Health and the National Health Group Domain Specific Review Board.

**Results:** All three patients were diagnosed with schizoaffective disorder on discharge, but the information from the medical records did not support this diagnosis. Two patients did not have clear records that they had at least 2 weeks of psychotic symptoms without mood symptoms. One patient had mainly schizophrenic symptoms most of the time. We found that two patients might have bipolar disorder and one patient might actually suffer from schizophrenia.

**Conclusion:** This study demonstrates that the clinical use of the schizoaffective disorder still has some limitations. There still remains a lack of consensus regarding the conceptual and clinical aspects of schizoaffective disorder. Since distinctions between the diagnostic categories of schizophrenia, schizoaffective disorder and bipolar disorder have been reported to be not clearly demarcated by findings from neuropsychological, neuroimaging, molecular neurobiology, or genetic epidemiology studies, schizoaffective disorder may exist on a spectral continuum between schizophrenia and bipolar disorder. Clinicians need to be cautious when diagnosing patients with schizoaffective disorder. Since the treatment guidelines for schizophrenia and bipolar disorder are well established and are substantially different, an overuse of schizoaffective disorder may encourage non-evidence based polypharmacy which may not be of benefit to patients.

**References:**
PP50 | School-based human sexuality education: Issues and challenges
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Introduction: The aim of the present study was to explore the way that educators evaluate their involvement in implementing health education programs in schools regarding human sexuality on the basis of “positive” or “negative”. A meta-analysis of the results of a survey on educators that implement sex education programs was conducted.

Methods: For the purpose of the present study, a qualitative approach was adopted. Data for this study was collected through half to one hour, semi-structured interviews with each informant. Study sample participants included thirty-three teachers of Lyceum who had delivered health education programs regarding sexuality and were from the region of West Greece. Verbatim transcripts of audiotapes were the primary data used in the content analysis.

Results: Educators choose to implement health education programs related to Human sexuality because these programs are primarily important to them. The implementation of sex education programs is of great significance for educators on a personal and not professional basis. Our study suggests that educators being involved in the implementation of health education programs related to human sexuality seemed to have a positive evaluation of their experience to the extent that the positive aspects were more important than the negative.

Conclusions: From the answers of our study sample participants, a huge discrepancy is highlighted between what should happen taking into account the related body of knowledge of the international literature and what really happens regarding the reasons why educators actually choose to implement sex education programs. While this kind of programs should aim to fulfill the needs of the students, it was found that sex education programs primarily fulfilled the needs of educators. We must be aware of this phenomenon in order to study it and to reduce it in order to make health education programs regarding human sexuality more effective and goal oriented.

PP51 | The challenge of the implementation of human sexuality education programs in Greek schools
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Introduction: Health education programs in schools regarding sexuality and sexually transmitted diseases may help all young people to take ownership of the means by which to make choices and to adopt behaviors that are responsible, both towards themselves and towards others and the environment around them. The aims of this study were to explore and analyze the reasons why teachers of Lyceum avoid being involved in the implementation of Sex Education programs.

Methods: For the purpose of the present study, a qualitative approach was adopted. Data for this study was collected through half to one hour, semi-structured interviews with each informant. Study sample participants included thirty-three teachers of Lyceum who had delivered health education programs regarding sexuality and were from the region of West Greece. Verbatim transcripts of audiotapes were the primary data used in the content analysis.

Results: Sex education is not one of the health education topics that educators involved in health education programs prefer to implement. They prefer to become involved in implementing health
education programs related to other topics that they could manage more easily. More specifically, educators avoid implementing health education programs related to sexuality for morality reasons.

**Conclusions:** Health policy should promote the integration of sex education in schools and educators should be appropriately trained and well prepared in order to implement adequately and successfully sex education programs. It is the responsibility of both individual professionals and health administrative leaders to take the necessary interventions to achieve the aforementioned goals.

**PP52 | Mirror neurons: Basic properties and functional role**

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**Introduction:** Mirror neurons (MNs), first discovered in the ventral premotor area F5 of the macaque monkey, are a class of neurons that respond during the execution as well as the observation of goal-directed motor acts. Two decades of research confirmed the existence of a parieto-frontal MN circuit in the macaque brain. Neuroimaging studies indicate that this MN circuit is also present in the human brain. The aim of this study is the investigation of the basic properties and of the functional roles of MNs.

**Methods:** Extra-cellular recording of 192 neurons during both execution and observation of the same movement (grasping an object), in the ventral premotor area F5 of a macaque monkey. We studied how MNs react at 5 different object shapes, their response time and if subject's attention affects their response.

**Results:** During our experiments, 106 neurons were activated both during the execution and observation of movement (typical MNs) and 31 of them were activated before grasping the object (early MNs); 11 ceased or decreased their response during movement observation (inhibitory MNs). The shape of the object and subject's attention did not affect the overall neural response.

**Conclusion:** MNs encode the goal of the action, contribute to motor learning and understanding of the meaning of movements made by others. The observer understands the movements of others, creating an internal representation of the observed movement and activating his own motor system like he was performing that movement himself; that's a procedure called **mental simulation**. In MNs may be lying the neurobiological basis of **empathy**. The clarification of the functional role of MNs will contribute to the understanding of neurodevelopmental syndromes such as autism (where it is known that the mirror complex is dysfunctional) and neurological conditions such as Parkinson's disease. Action observation training (which activates the MN circuit) is beneficial to attention, movement skills and facial recognition in patients that suffer from Alzheimer's; thus holding potential for being a method of slowing its progress.

**PP53 | Potential drug-drug interactions in patients with psychiatric and cardiovascular comorbidity**


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**Introduction:** Drug-drug interactions in patients suffering from cardiovascular disease and psychiatric disorder present a serious clinical problem in general hospital. This study aimed to identify putative drug-drug interactions in these patients since both categories of drugs were augmented to them.
**Methods:** One hundred patients evaluated by Consultation-Liaison Psychiatry were surveyed. Patients with certain comorbidity (cardiovascular disease and a psychiatric disorder) were selected for evaluation. Medication records at patients’ submission were analyzed for the probability of drug-drug interactions between psychiatric drugs or between psychiatric drugs and drugs administered for cardiovascular abnormalities or other medical conditions. Drug-drug interactions were further categorized according to the clinical intensity of outcome in three groups: severe interactions that might be life threatening and must be avoided, such as arrhythmia; moderate interactions that are probably seeking the change of therapeutic medication and include efficacy issues as well as the necessity for frequent monitoring; and mild interactions in which there is no need reconsidering the therapeutic strategy and have minor side effects, such as somnolence. Furthermore, the mechanism of drug-drug interactions was taken into account, considering both pharmacodynamics and pharmacokinetics actions, mainly focusing on metabolism via hepatic cytochrome P450 correlated with the clinical intensity of outcome for each individual group.

**Results:** Among 100 patients surveyed, 30 patients had a cardiovascular disease and 15 had cardiovascular disease and a psychiatric disorder. The probability for a present drug-drug interaction was 86.67%, with 58% corresponding to interactions between psychiatric drugs and other drug classes and 42% representing interactions occurring only between psychiatric drugs. In terms of clinical intensity of outcome, the first case (psychiatric medication interacting with a separate class of drugs) gave rise to 58% moderate, 32% mild and 10% serious interactions. Sixty two per cent were pharmacodynamic interactions further characterized as moderate (55%), mild (35%) and serious (10%). Also, 38% were pharmacokinetic interactions including moderate (59%), mild (33%) and serious (8%). According to potential interactions between psychiatric drugs, mild (77%), moderate (14%) and serious (9%) were identified. Eighty four per cent comprised of pharmacodynamic interactions which were further subdivided into mild (83%), moderate (11%) and serious (6%). Sixteen per cent were pharmacokinetic interactions, moderate (50%), serious (25%) and mild (25%).

**Conclusion:** There is a high probability of drug-drug interactions in patients with cardiovascular and psychiatric comorbidity. Most of the drug-drug interactions identified in this study were between psychiatric drugs and other drug classes, mainly those which were augmented for the cardiovascular abnormalities. Therefore, there is need for a frequent monitoring of these patients and usually for a reconsideration of their medication strategy. A systematic cooperation of cardiologists and psychiatrists in these patients treatment approach could provide the best care for them.

**PP54 | Potential drug interactions in patients evaluated of consultation liaison psychiatry**


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**Introduction:** The prevention of potential psychiatric drug interactions in patients referred to consultation liaison psychiatry, who have a psychiatric disorder and are on medication at their submission in the general hospital, has a severe clinical importance.

**Methods:** One hundred patients of Consultation-Liaison Psychiatry were surveyed and those presenting a psychiatric disorder were included in this study. Drug treatment at patients’ submission was further analyzed for a probability of drug-drug interactions between psychiatric drugs themselves. Drug-drug interactions were further categorized according to the clinical intensity of outcome in three groups: severe
interactions, that might be life threatening and must be avoided, such as arrhythmia; moderate interactions that are probably seeking the change of therapeutic medication and include efficacy issues as well as the necessity for frequent monitoring; and mild interactions in which there is no need reconsidering the therapeutic strategy and have minor side effects, such as somnolence. Furthermore, the mechanism of drug-drug interactions was taken into account, considering both pharmacodynamics and pharmacokinetics actions, mainly focusing on metabolism via hepatic cytochrome P450 correlated with the clinical intensity of outcome for each individual group.

**Results:** Among one hundred patients surveyed, 50 had psychiatric disorder with an average age of 57. The probability for a present drug-drug interaction was 56%. In terms of clinical intensity of outcome 79% were mild interactions, 11% moderate and 10% severe interactions. Eighty per cent of them were pharmacodynamic interactions which were further separated into 89% mild interactions, 7% moderate and 4% severe. Also, twenty per cent were pharmacokinetic interactions which were including 40% serious, 35% moderate and 25% mild one.

**Conclusions:** The most potential interactions between psychiatric drugs at patients submission were found to be pharmacodynamic and mild. The pharmacokinetic interactions were fewer but most of them serious. In conclusion, one in ten potential interactions were found to be serious and should be avoided.

**PP55 | How the treatment with depot affects compliance**

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**Introduction:** The care of the mentally ill is undoubtedly a long healing process that brings high costs to the National Health System. In each treatment the high compliance of the mental patient plays an important role so as the state costs to be reduced and to be observed improvement at patient's state of health. Compliance helps in reducing relapses and predicts better the patient's health. In patients with severe psychosis and stabilized customarily administered injectable antipsychotics long lasting (depot) to prevent relapse, as successive relapses affect the life quality of the patients.

**Methods:** The purpose of this study is to examine the conformity of psychiatric patients with depot treatment. 20 psychiatric patients at the General Hospital of Nikea completed two questionnaires self-report on the evaluation of conformity: the Medication Adherence Rating Scale (MARS) [1] and Personal Evaluation of Transition in Treatment (PETiT) [2]. Also, the supervisor whenever treating completed a compliance level evaluation of each patient Clinical Rating Scale (CRS) [3]. They obtained demographic information and information on the treatment, its probable interruption and mass index of the patients body.

**Results:** The age of patients was on average 43.3 years (±10.60), while in the diseased on average was 16.50 years (±6) and in receiving depot injection therapy was on average three years (±1.41). Only 40% of patients received treatment in depot form, while 60% received combined depot and perros. 55% of participants had graduated from tertiary education and 70% of them was unmarried. The analysis of the results proposes that those who discontinued treatment for a period of 3-9 months exhibited alongside low compliance in their injectable treatment (two patients relapsed, one changed treatment context, one relocated). Since the inductive analysis detected differences among individuals encountered or not encountered difficulties in injecting treatment and evaluation by the physician $t$ (18) = -5.06, $p < .001$. In addition there was a positive correlation between the time period the individuals receive injecting treatment and their compliance in accordance with both MARS questionnaires ($r = .459$) and PETiT ($r = .452$).
Conclusion: The compliance of patients on injectable treatment is associated with the various difficulties the patients confront with and the years of therapy. As a consequence, people who had difficulties in their treatment are likely to show lower compliance comparing to people who received injectable treatment and show better compliance. The increase of psychiatric patient compliance aims to reduce relapse, improve the state of their health and cut down public funds. Conclusively, it is evident how significant role can play those conditions which will enhance compliance of psychiatric patients even from the very beginning of the therapeutic intervention.

References:

PP56 | Development and validation of a skin fibroblast biomarker profile for schizophrenic patient

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Introduction: Gene expression profiles of peripheral cells through microarray technology could be used in schizophrenia studies, adding more information to the results from similar studies on postmortem brain tissue. The ultimate goal of such studies is to develop an accessible peripheral biomarker. We performed supervised methodologies, in order to examine if the gene expression signature from skin fibroblast cells could separate schizophrenic from healthy control samples.

Methods: A dataset of skin fibroblasts gene expression profile of schizophrenia patients was obtained from GEO database of NCBI. After applying RMA preprocessing and then moderated t-test with the following criteria: (a) 0.3-fold or greater change in the mean expression level and (b) p-value <0.05 after correction of multiple testing with the False Discovery Rate (FDR) adjustment of Benjamini and Hochberg, we concluded to 63 genes that present a differential expression between the schizophrenics and the healthy controls. Based on those genes, functional profiling was performed with the Bioinfominer web tool. The differentially expressed genes were also used as an input for training several machine learning classifiers.

Results: The functional profiling revealed interesting terms and pathways, such as MAPK- and cAMP signaling pathways, immune-related pathways and brain size abnormalities. Support Vector Machines outperformed all the examined classification algorithms. Additionally, a subset of 8 differentially expressed genes from fibroblast gene expression profiling, could separate schizophrenics from healthy controls in an independent postmortem brain dataset.

Conclusion: These findings suggest that through the analysis of a fibroblast based gene expression signature we might conclude to a diagnostic classification model in schizophrenia.
PP57 | Challenges and recommendations of ElectroConvulsive Therapy (ECT) in heart transplant patients
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Objective: Heart transplant patients may face depression before and after a transplant (Jones, 1991). Electroconvulsive therapy (ECT) is a treatment for a wide variety of psychiatric conditions. As the practice of modern ECT continues to evolve, results of research consistently demonstrate this to be a treatment with significant efficacy and safety. As ECT uses an electrical current to produce a seizure, some practitioners may be hesitant to use it in patients who have a history of heart transplant surgery (Bloch et al., 1992). We present a case of a 68-year-old Caucasian male who recently had an orthotopic heart transplant and successfully tolerated and responded to six ultrabrief right unilateral (UB-RUL) ECT treatments. Methods of modifying ECT to treat patients after a heart transplant will also be discussed.

Methods: A case report of a geriatric patient that was status-post orthotopic heart transplant and who was successfully treated with UB RUL ECT. We will also present a review of literature on this topic (Lee et al., 2001).

Results: 68-year-old Caucasian male with significant depression, postoperative confusion, and a suicidal plan to shoot himself with a gun. Primary team prescribed escitalopram 20mg qday with no response. Olanzapine was given for post-operative confusion. Patient failed mirtazapine in the past. No other prior psychiatric history. Family history was significant for two brothers dying by suicide. Due to his failure to thrive and his suicidal thoughts with expressed plan the ECT service was consulted for the consideration of ECT. Six UB-RUL ECT treatments resulted in improvement of depressive symptoms and confusion.

Conclusions: While literature is significantly limited on this topic, our case demonstrates the promise of ECT in treating depressive symptoms in geriatric patients who have undergone a heart transplant. This case also brings to light the importance of doing a thorough psychiatric assessment on patients prior to performing a heart transplant (Fusar-Poli et al., 2006). It could be argued that if psychiatry was consulted earlier, the patient's outcome may have been more favorable.

References:

PP58 | The free will problem: Between neuroscientific determinism and freedom
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Introduction: In his famous book “The Doors of Perception” Aldous Huxley raises the following question: is a mental disorder or some other cognitive incident the result of a chemical disorder? Accordingly R.S.De Ropp in his book titled “Drugs and the Mind” confirms that neither the thought nor the sentiment could emerge without a chemical alteration in our brain. Assuming that the above are true should we suppose
that we act in a truly free manner or are we subjected to alterations outside our conscious control? The previous assumptions could serve as a starting point to reflect the most controversial issue not only of philosophy but also of psychology and neuroscience: the free will problem. We are wondering how it is related to certain concepts such as autonomy, rationality and responsibility which are very important to our self-image as human beings.

However the neuroscience of free will has challenged our intuitive experience through experiments that take under consideration the issue that it is only our free will that produces our actions by proving that the general structure that concerns the function of the agent as for the exercise of his free will is related principally to neurobiology.

Determinists believe that human beings are biological machines whose actions are absolutely definite; thus they refuse any aspect of human freedom and moral responsibility. They maintain that the agent is determined by incidents which emerge into his brain and which have been brought about by former inner and external events. Libet’s experiments from 1983 and more recently the relevant ones of John-Dylan Haynes have proved that our free will is not an actual phenomenon but it is a brain function that exists beyond our consciousness; our brains are deciding for us and these decisions are beyond our control.

But, if our decisions are not in our control, how could we be regarded as moral agents? Supporters of libertarian account consider that a free decision or an event being into the inner part of a decision should be caused by the agent and that this decision should not be provoked by other causes or facts. Actions consist of a conscious choice as a part of awareness of the objectives and the consequences and by extension the awareness of moral responsibility which corresponds to the outcomes of his actions.

**Conclusion:** The aim of this paper is to highlight the range of opinions about the free will problem by depicting experimental data and theoretical implications in order to indicate that the scientific description is not the only one available through which an action is assessed as we should not encounter human agency in a materialistic way.

**References:**
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