European Association for Mental Health in Intellectual Disability, 2017. Luxembourg 21-23 Sept, Conference report.

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The European Association for Mental Health in Intellectual Disability (EAMHID) must be one of the largest international, multidisciplinary, organisations that focuses on mental health in people with intellectual disability (ID). In 2017, it's conference was held at the European Convention Center, in the modern Kirchberg Plateau development of Luxembourg. Luxembourgish is the official local language, but most debate is had in French and the papers are published in German. Primary school is taught in German and High School in French. These are the presentations that stood out for me from the conference.

Mental Health and Intellectual Disability

Nick Bouras a founding member from King's College and the Institute of Psychiatry, London, spoke on EAMHID, its history and developments in evidenced-based practice. EAMHID was only founded in 1990, at a time of de-institutionalisation and uncritical acceptance of the social model. Across Europe there is wide disparity in service provision, which is generally worse in low and middle-income countries. This includes marginalisation from mainstream employment, limited access to mental health services and a lack of professional training. There has been a growth of research and epidemiology but it is seldom published in mainstream psychiatry journals and relies on the Association's 3 journals.

Bouras commented that data shows MH problems in ID are common, are associated with negative outcomes, that interventions need strengthening and that services are fragmented. He continued that we need large multicenter studies and outlined the barriers including who will fund MHID research? In USA 67% and Europe 74% of people with MHID don't receive services, compared with physical health where for example only 8% with diabetes don't receive services! Yet there is now a global MH movement, not necessarily including ID. We need to set priorities, define intervention packages, and identify countries that need to do more. We need to define the role of specialists, and increase training and supervision.

In September 2015, the UN 2030 Agenda for Sustainable Development included for the first time the promotion of mental health, not just physical health and the prevention and treatment of neurodevelopmental disorders. There is a right to quality MH care for every person with ID which includes assessment, comprehensive diagnosis and individualised treatment in the right place, time and appropriate social setting.

Why do children with ID have such high rates of behaviour disturbance?

Vaso Totsika from the University of Warwick presented data from a huge cohort study on the effect early adversity has on parenting and its relationship to behavioural disturbances in children with learning difficulties (LD). Testing used the Family Stress Model of Conger and Donnellan, which views families as systems in which children grow, and that negative behaviour comes from negative processes, which are associated with poverty, parental stress and child behaviour problems. But how do these risk factors work together? This has been studied in typically developing (TD) kids, but not in those with LD. They studied 555 families of children with LD (identified by a British Assessment Scale at 7 years) compared with 19,000 families of TD children from the Millennium Cohort, assessing parental adversity at 9 months and outcomes at age of 7 and 9 years. Parental adversity at 9 months was a poverty measure derived from below income poverty threshold, mean durable assets, family struggling financially and unavailability of grandparent support. This early parental adversity was related to emotional problems, hyperactivity, conduct problems and total behaviour problems at age of 7 and 9 years. However, positive parenting significantly reduced the association with behaviour problems, hyperactivity and emotional problems. The parenting was measured age 3 and 5 years. Adverse parenting was based on observations of: frequent discipline, conflict in the relationship and harsh parenting. Positive parenting was measured by observations of closeness and parental positivity. Accordingly, in children with LD, behaviour problems are mediated through adverse parenting and not by positive parenting. They conclude that to prevent behav-

Above: The Golden Girl of Luxembourg commemorating those lost in the first World War.

iour problems in LD, we need to reduce poverty, have universal screening of post-natal depression and provide universal parenting programs and specialist parenting intervention for children with LD (ID).

The importance of early intervention through parent training

Kylie Gray, Director of Monash University Developmental Psychiatry, presented initial data on the MySay project following the widespread implementation of Stepping Stones Parent Training (SSPT) across east coast Australia, with an aim to make a difference at a public health level to behaviour problems in children with ID. SSPT was provided to parents of children aged 2-10 years with developmental delay or ID. 251 professionals were trained in SSPT in Victoria and Queensland. 365 families received intervention with 3 and 12 months follow up. Both children with ID and ASD showed and maintained improvement in behaviour. Parenting with higher levels of coercion and inconsistency was associated with greater behaviour disturbance, and those with higher levels of coercion had smaller improvement, however where there was a change in coercive parenting style there was greater change in childhood behaviour. Both these studies reenforce the need to tackle adverse parenting.

MH problems in children with ID: a mainstream policy issue

Richard Hastings Cerebra Chair of Family Research at the University of Warwick presented on MH problems in children with ID: a mainstream policy issue. The UK Office of National Statistics surveyed 18,000 children aged 5-16 years and identified 3.5% (or 641) as 'likely to have ID'. Emerson and Hatton (2007) found those with ID had 36% psychiatric disorder (vs TD controls 8%), with emotional disorder 12% (3.5%), Hyperkinesis 8% (1%), and conduct disorder 22% (6%). Conversely 1 in 7 children with a mental disorder have ID. The Millennium Cohort Study identified 479 (3%) 5-year olds on British Disability Scales with ID. At 5 years of age, 48% were hyperactive (vs 15% TD controls), 40% had conduct disorder (22%) and 28% had emotional disorder (10%). The risk factors associated with MH are: single parent 30% (23%), poverty 47% (30%), 2 or more negative events 27% (18%), and a carer with no educational qualification. Three or more risk factors were found in 46% of children with ID vs 24% of typically developing children. Other factors identified as important: genetic and biological factors, difficulty recognising/labelling emotions, limited communication skills, poorer quality close relations, lack of diagnostic recognition, lack of access to services (only 29% accessed MH services in last 6 months). NICE guidelines identified an inequality in evidence, with fewer studies of parenting programs in children with ID, and what studies there are, show positive but less effect than in TD.

Challenging Behaviour (CB): Individual Difference Matters

Chris Oliver, Chair of Cerebra Centre for Neurodevelopmental Disorders, University of Birmingham, gave an exciting presentation based on research of behavioural phenotypes 'Challenging Behaviour (CB): Individual Difference Matters'. Using seven different behavioural phenotypes they propose that aggression (Agg) and self-injurious behaviour (SIB) has different causal mechanisms. It is also important to recognise

> "Significant advances in evidence that children with ID develop higher rates of emotional and behavioural disturbance"

dimensional severity. For example, both Autistic Spectrum and Autism found present in Fragile X in 80% vs 45% and in Smith Magenis Syndrome (SMS) 70% vs 30%. He talked about five important and different etiological pathways to CB: 1. physical disorders and sleep; 2. social drive and cognition; 3. cognitive and executive function; 4. emotional variation of anger and anxiety; and 5. sensory sensitivity and perception. For physical disorders, they use a behavioural pain and discomfort questionnaire, Face, Legs Activity, Cry & Consolability (FLACC) (Malviya, Voepel-Lewis, Burke, Merkel, & Tait, 2006), such as identifying gastro-esophageal reflux with SIB in Cornelia de Lange's Syndrome, or the Sleep problems of SMS using Actigraphy, which shows them awake at 2am. 2. Angelmans Syndrome have higher social approaches but also aggression. They found higher aggression in low attention settings. Wilder showed with the Ainsworth Stranger Situation Test that those with SMS have a strong attachment to their mother and low interest in a stranger when compared with Down Syndrome are more likely to be distressed with mother's departure. 3. Repetitive behaviour and impulsivity are two elements of executive dysfunction in addition to ID. Repetitive behaviour predicts aggression in Fragile X, whereas impulsivity predicts aggression in SMS and Angelmans. They used go-no-go tasks to assess executive function. Prader Willi Syndrome (PWS) have increased reaction time after a shift paradigm, and this result correlates with repetitive questioning and adherence to routine. 4. Both Fragile X and PWS have high emotional response to an aversive stimulus. Lowes Syndrome have high impulsivity and high emotional output, which is associated to low executive function on the BRIEF.

Oliver concluded that ID leads to compromised learning and behaviours. Behaviours are related to other underlying deficits. Accordingly, the term challenging behaviour may have outlived its usefulness, as individual neuropsychiatric qualities need consideration. For example, people with PWS shouldn't be considered as obstinate, but the reaction times show that change of attention is harder for them.

Over all I was struck by the significant advances in evidence that children with ID develop higher rates of emotional and behavioural disturbance. There is also evidence that a lot can be done, particularly while a child is still under 10 years of age, to prevent and improve this challenging behaviour. Is anyone listening?

Psychopharmacology workshop: a brief overview of the evidence, theory and prospects.

Marco Bertelli, psychiatrist from The Research and Clinical Center, San Sebastian Foundation, Florence, President of the Italian Society for Neurodevelopmental Disorders and Past President EAMH-ID presented an innovative workshop on pharmacology in adults with ID. However, this presentation although strictly evidenced-based, was quite specialised and somewhat theoretical. 20-45% of people with ID receive psychoactive medications. Two thirds are on antipsychotics, 20% of those in a residential facility and 45% of those hospitalised. 45% of adults with ASD are on medication. Paton and Flynn (2011) study of 39 centres and 2319 clients found 27% had a psychotic disorder, 27% an affective disorder, but 6% with borderline IQ and 21% with severe/profound ID were on antipsychotics without a psychiatric disorder. In people with ID, 50% are taking antipsychotics for problem behaviour. Documentation was good, but the monitoring of side effects was less careful.

At Salford Disability Service (Griffith et al, 2012) of 178 patients, 72% were on antipsychotics of which 11% were on 2. 67% had a psychiatric disorder, 33% were prescribed for 'off label' reasons. 64% were initiated by a GP, 28% an unknown prescriber, and 8% a GP or pharmacy alone. There are diagnostic problems in defining MH in ID: difficulty in defining the additional impairment and difficulty in determining the level of distress or suffering. There is an overlapping genetic vulnerability for ASD, ID, Schizophrenia, Bipolar and Depression, and epigenetics play a role. Additional diagnostic problems include: Intellectual distortion (ie affected by communication skills and IQ; developmental appropriateness; psychosocial masking (ie cultural, interpersonal and environmental distortion); ID diagnostic overshadowing; atypical presentations eg aggression, maladaptive behaviour; neuro-vegetative vulnerability eg somatic complaints, circadian rhythms, nonverbal dystonias; cognitive disintegration. Life problems are common, about 60% have at least 1 life problem, with aggression, irritability, self-injury, hyperactivity, impulsivity, sleep problems and repetitive behaviours. The 2-year remission rate for SIB is 38% and Aggression is 27%. Conversely the 11-year persistence rate is 79% for problem behaviours, 70% for aggression, 65% for stereotyped behaviour, 49% for SIB. Per-

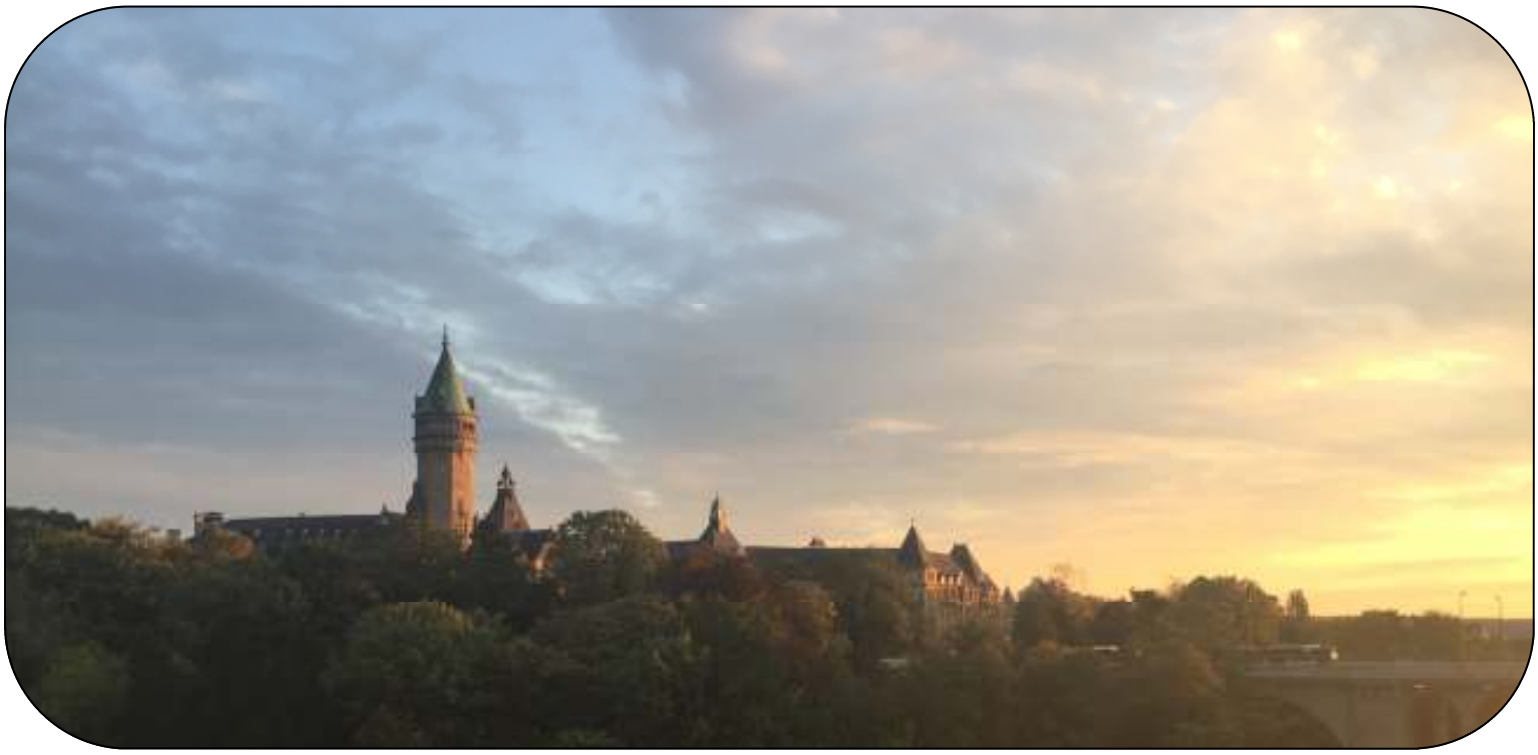
sistence particularly occurs in ASD and adults. Some authors suggest some behaviours may be symptom equivalents, other suggest they are a sign of distress. Can this all be attributed to the lack of competence of the multidisciplinary team? Before prescribing one should consider a functional analysis, the influence of ID/developmental level and organic factors.

He summarised the vastly *different types of antidepressants*, many that are novel, and their mechanisms and attempts to provide a rationale for their different effects and when to use them: SSRIs: GPs use citalopram or fluoxetine. Fluvoxamine has less impulsivity as a side effect, and has greater effect in young adults, related to 5HT transporter polymorphisms, but literature suggests more side effects. He prefers Escitalopram. Escitalopram and citalopram improve anxiety, irritability and mood. Of the SNRIs (selective noradrenaline reuptake inhibitors), he prefers duloxetine over venlafaxine because of side effects of sexual dysfunction and obesity, although there is no literature in ID. He published a case report of complete remission of globus hystericus (difficulty swallowing) with duloxetine. NDRI (noradrenalin and dopamine reuptake inhibitors) (buproprione) and NRI (reboxetine and atomoxetine): one study of atomoxetine in Williams Syndrome was less effective than Ritalin with greater side effects such as stomach pain and irritability. NaSSA/SNRI-alpha2 agonists also activate Histamine1: include Mirtazapine, Mianserin, Quetiapine and Asenazepine. SARI (Serotonin agonist uptake inhibitor) such as Trazadone and Nefazolone, are an alternative to benzodiazepines, and good in the elderly with CB with anxiety, irritability and activation. Agomelatine affects the melatonin system and helps in neuro-vegetative states, dystonia and somatic anxiety; in animal models, it improves sociability in ASD, but the evidence is yet lacking in humans.

Recent research links the serotonergic system with the glutamate system. Glutamate receptor 5 affects synaptic plasticity and synapse formation and GlucR5 receptor down regulation can prevent intellectual disability eg in Tuberose Sclerosis. Bumetanide (a chloride importer antagonist) in one study improved ASD. Memantine (antagonist to NMDA receptors) in an open label study improved social withdrawal, inattention, hyperactivity, and memory in ASD. Acamprosate (a gaba A agonist and excitory glutamate antagonist in an open label study improved social withdrawal, hyperactivity and social responsiveness in ASD. Lorastatin and Acamposate helped in Fragile X, as did minocycline and sertraline particularly in the first 5 years. Vortioxetine is a new agent which blocks the serotonin transporter, is a 5HT agonist, removes Gaba and stimulates glutamate which has improved cognition in the elderly with depression. Ketamine is another glutamate antidepressant. He suggests that depression can be split into: 1. Noradrenaline and 5 HT (serotonin) deficits which are associated with negative affect with irritability, anxiety and sadness and responds to SSRIs, SNRI and SARI. 2. Deficits in dopamine and noradrenaline is associated with reduced positive affect along with somatic symptoms of reduced energy, sleeping, eating and stress and responds to NDRI SNRI, NRI, modafinil or a stimulant. 3. Is the combination of 1&2 and needs SNRI or SSRI plus NDRI.

He further breaks affective disorders into main groups: Prominence of physical symptoms: from low 5HT and

Below: The Battlements and Spires of Luxembourg



noradrenaline needing SNRI and pregabalin and gabapentin (alpha 2 stimulation);
Hypersomnia needing stimulant and histamine;
Prominence of emotional symptoms/anxiety needing 5HT and gaba with SSRI or SNRI;
Vasomotor symptoms from low 5HT and noradrenalin needing SNRI and possibly oestrogen; Sexual dysfunction from low dopamine, needing NDRI. There is a growing trend of using more than one antidepressant to enable different antidepressant effects through such multimodal treatment, rather than resorting to other augmenting medications.

Antipsychotics: There is better evidence of the benefit of new generation antipsychotics (NGAs) in improving problem behaviour than with traditional antipsychotics. They also have fewer side effects. Both Risperidone and olanzapine are shown to work. Risperidone, Aripiprazole have FDA approval for irritability in ASD in children and adolescents. Risperidone has greater effect with topiramate or memantine on irritability, hyperactivity and stereotypic behaviour. Main side effects of increased appetite and weight, sleepiness and high prolactin. Paliperidone is similar to risperidone except it is not metabolised in the liver.
Olanzapine is effective in case series for aggression, SIB and disruptive behaviour.
Aripiprazole helps aggression, SIB, tantrums and mood changes in ASD and shows effectiveness vs placebo across the lifespan. Recent open label study showed effectiveness on Fragile X.

Asenapine has a bigger effect on serotonin and therefore may need a higher dose to work on dopamine. Useful alone or with valproate or escitalopram. Ziprasidone has evidence of utility in problem behaviours but has the advantage of being weight neutral.
Clozapine has been used in problem behaviours. If you get neutropaenia you can restart after a one month break. Clozapine and NGAs cause early synaptogenesis through microglia and removal of redundant and maladaptive synapse. There is growing understanding of additional effects of NGAs including additional neurotransmitter effects eg blockade of NMDA agonists, increase in gaba neuro-steroid allopregnanolone, increased neurotrophic effects eg increase in neurotrophic factors eg BDNF, increased neurogenesis, preservation of acetyl choline neurones and cognitive function, and increased cell protective functions eg increased antipoptopic proteins, anti-oxidants, and mitochondrial respiration.

While there is growing demand for pharmacological knowledge and solutions, the evidence is slow to accumulate and depends mainly on case series. I think that critics have little idea of the harm and distress caused by extreme problem behaviours or CB. Conversely there are real concerns of the failure of general medical clinicians and GPs to provide follow up and ongoing monitoring, so when studies are done to try and withdraw a NGA, it is found that 50% do not need continuing medication (but 50% still do).

Mood stabilisers include valproate for irritability, aggression and stereotyped behaviour; lamotrigine (blocks the release of glutamate) for anxiety and depression and Levetiracitam which has one open label study improving mood stability and aggression.
Melatonin has accumulated good evidence of benefit in sleep disorders over the last 5 years.

His presentation reminds us that psychiatrists have to keep up to date with the ever-expanding theory and research arising around new medications. One also needs to watch out for exploration into neuroceuticals such as theanine, an analogue of glutamine, found in tea and helps cognitive function, sleep, menstrual pain and stress; passion flower extract may have gaba effects and benzodiazepine like properties; and N-Acetyl Cysteine which may have effects on PTSD in war veterans.

The beautiful artworks in this journal are taken from the participants of the **Operation Art project** at the Children's Hospital at Westmead. You can find out more at https://www.artsunit.nsw.edu.au/visual-arts/operation-art-2014

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