The 15th World Congress of the International Association for the Scientific Study of Intellectual and Developmental Disabilities (IASSID) Melbourne 15-19/8/2016.

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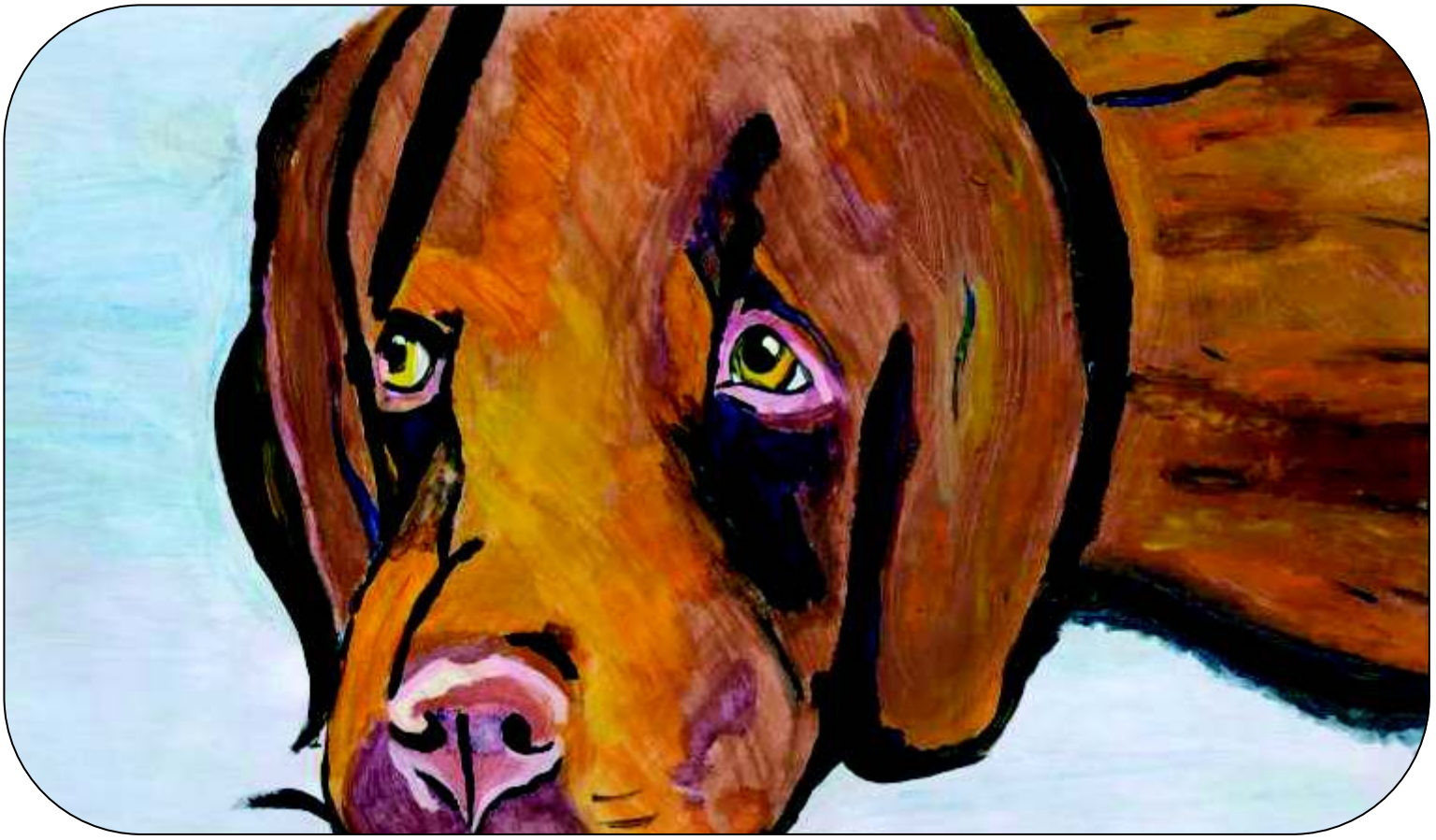
1300 people congregated in Melbourne for 15th World Congress of IASSID, a conference of both science and humanism, from the latest understanding on genetics, and mechanisms of the mind, to the importance of recognition and inclusion of people with intellectual disability, to sessions on spirituality and quality of life.

With 14 parallel streams there was plenty to choose from and different attendees experienced a totally different conference, although this was punctuated with plenaries and master lectures. Abstracts are published in Journal of Intellectual Disability Research 60: (7&8). The poster session with cocktails was a great source of networking with the international family of professionals in ID. Mental health was a more central theme than in the past, and indeed was children and adolescents. There were several messages indicating the importance of recognising mental health needs as something always to be considered separately to an intellectual disability, and an increased identification of pathways to wellbeing and achievement for example in people with Down Syndrome where inclusive education can lead to better self esteem, employment, participation and a positive wellbeing. Forrester-Jones reported on how faith-based spiritual organisations were more inclined to consider the spirituality of their clients with ID and in turn this led to clients having twice the size of social networks.

Here are a few of my highlights:
Jozef Gecz, from the Women and Children's Hospital in Adelaide gave an impressive update on the 'genetic architecture of neurodevelopmental disabilities (NDD)'. His presentation highlighted how rapidly our understanding of genetics is changing, increasing our understanding of interactions between the complexity processes and the huge diversity of outcomes. He has been party to identifying 100 genetic disorders particularly of the X chromosome. He reminded us that the rate of developing genetic knowledge is remarkable: DNA discovered in 1953, first human genome sequenced in 1999, now a 1000 genomes are being sequenced a day and soon for $1000 (although the opinion costs more). We have 21,000 coding genes which is 2% of the genome, but the 'junk' ('non coding DNA') 98% may also be important, partly as the spacing can be important, but individual junk genes may have enhancing or modifying roles. For example, in a gene wide association study (GWAS) of obesity, a junk region gene related to enhancing white or brown fat. Some enhancer (but not coding) genes work through transcription factors. Eric Green predicted that the human genome would change the delivery of medicine, but currently cost prevents equity of access. We are 99.6% genetically identical with each other, 98% with a chimpanzee and 90% with a mouse. Deletions and insertions account for 15% of abnormalities. Everyone has 3-7 copy number variants (CNV).

Fragile X was discovered in South Australia and remains the most common identifiable cause of ID. The X chromosome has 800 genes of which 1/5 is involved in genes linked to ID. The proportion of people with ID that have a genetic abnormality has gone up to 62%: 12% have abnormality on chromosomal micro analysis, 27% on whole exome sequencing and 42% on whole genome screening, including CNVs and single nucleotide polymorphisms (SNP). Various epilepsies are genetic, but different mutations of the same gene can cause different NDDs. Conversely loss of a functioning gene doesn't always cause disease. Indeed, the same gene can have variable outcomes. Some cause several disorders, with different penetrance and environmental modifiers. BDNF (brain derived neurotrophic factor) polymorphism is a protective factor e.g. in Retts Syndrome. Nonetheless genetics explain 75% of the variance of educational progress. The Global Genetic Exchange helps identify single cases of ID. Gene DDX3X causes hypertension, movement disorder and behaviour problems, but is also a target for cancer treatment. There is an interesting overlap of 250 genes between NDDs and cancer. Most cancer genes are also involved in NDDs because they are involved in cell/neuronal proliferation and synapse formation. When one thinks that every cell has the same DNA, then the differentiation of structure and

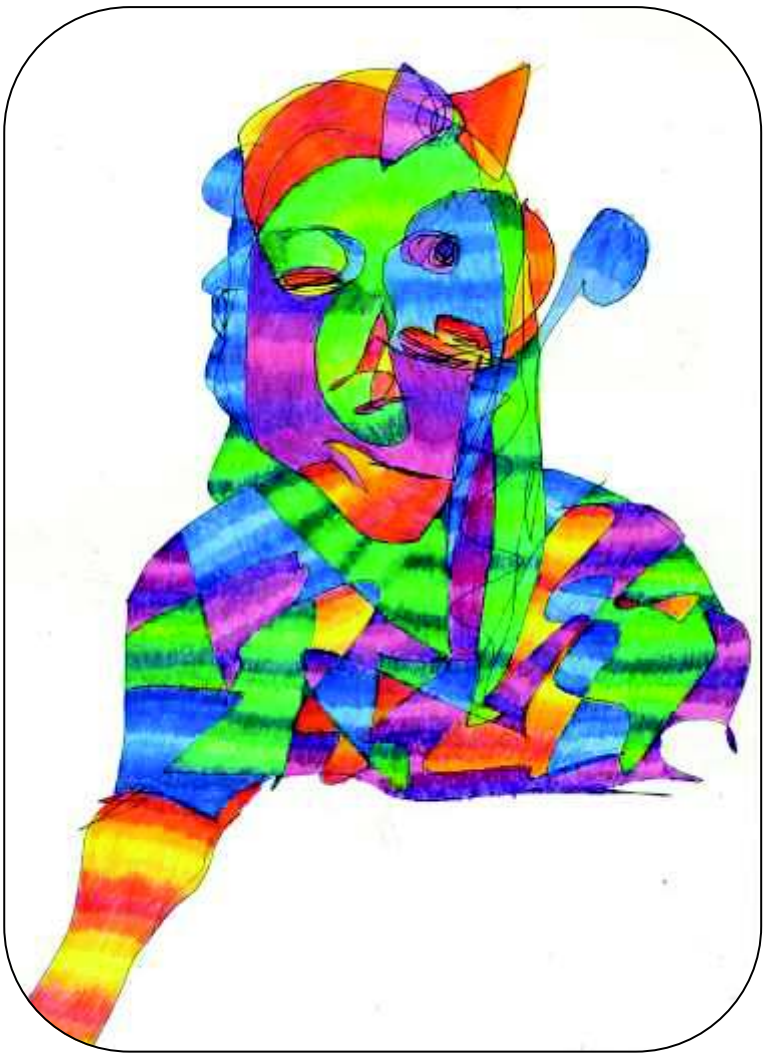


function is due to enhancers and modifying genes/ processes.
He talked about PCDH19, a genetic deletion that leads to cluster epilepsy in girls. They appear to be healthy for 9 months, but regress developmentally with stress or infection and 62% have NDDs and 30% ASD. There seems to be a brain signaling problem involving androgen/progesterone, affecting GABA receptors and BDNF. They are deficient in allopreganolone which is a brain steroid that is protective in PTSD, ASD and seizures. A novel neural steroid medication, Ganaxolone is being trialed with some benefit. Boys aren't affected because of a knockout effect of the gene, whereas the girls have two types of cells, some that are functioning and some that aren't.

We now know 700 different genes contribute to ID, 300 in Epilepsy, over 800 in ASD, 120 in Schizophrenia and over 20 in Cerebral Palsy (CP). However, there is huge overlap between the genes involved in NDDs such as ASD, ID, Schizophrenia, Bipolar, and Anxiety and more complex interactions between the genes, proteins and conditions. Many of these genes work at the synapse, and gene networks control the DNA, with environmental interactions. The gene TBCID24 can cause a NDD or deafness. A gene active in the perinatal period of brain development may become more active later in development. There has been no reduction in CP with the increase in rate of caesarians, indicating that CP is not due to perinatal insult. Indeed 14% have genetic findings, 10% de novo, 4% inherited and 40% more have candidate genes. A further 20% could be explained by copy number variants (CNV). Environmental factors such as substance abuse, or too much or too little food affect genes and these effects are passed onto the next generation. This is part of epigenetics. Even with rare conditions, large cohorts are needed to elucidate genetic processes. For example, in schizophrenia an increase in sample size from 50 to 150,000 identified, instead of just 5 genes, 120 relevant genes. The heritability of Schizophrenia is 80%, Bipolar Disorder 60% but recent studies have brought it down for ASD to 50-55%. Some of these genes map to the immune system, for example complement 4A CNV increases pruning of neuronal dendritic spines. The Micro Biome of the gut also affects the human genome, e.g. in ASD development, including what we eat and what antibiotics we take. It is possible to transplant a metabolic syndrome with the Micro Biome. Some genetic metabolic syndromes can be treated. Ganaxolone has also been shown to improve Fragile X. Iceland now has a project to do the whole human genome on the total population. This presentation was impressive, as it introduces a much greater degree of complexity to genetic mechanisms. It may be that Fetal Alcohol Spectrum Disorder (FASD) is the archetypal epigenetic syndrome, partly by what alcohol does to moderator genes, and partly as some toxic effects from alcoholic in utero affect epigenetic processes and change development and behaviour in subsequent generations.

Irva Hertz Picciotto from the Mind Institute at UC Davis presented on the potential of environmental chemicals

to cause ASD. In California the incidence of ASD has gone up seven times in birth cohort studies between 1987 and 2002. Changes in diagnostic criteria, inclusion of milder cases and aging of the maternal population only accounts for a doubling. Prenatal exposure to toxins is important for neuronal development and migration. There is no single cause for ASD but outcomes are multifactorial. All factors only increase risk. Examples include lead poisoning, congenital rubella, thalidomide and valproate. Their 'childhood risk of environment' study is a case control study from 2002, looking at pesticides, heavy metals, organic pollutants, viruses and nutrients. Eg. Pesticides can interfere with GABA and Glutamine ion channels. Chorpyrifos change parts of the brain involved in social processing, memory and IQ. Maternal metabolic conditions cause an increase in a range of conditions, such as inflammation, diabetes, hypertension, ADHD and ASD. Folic Acid is required for DNA synthesis and methylation. There are then genetic risk factors that interact with such environmental factors. Their study is looking for 1000 chemicals in blood samples, but there are 10,000 new organic chemicals registered a year! Even when a toxin is found to be relevant it only has a small increased risk and it is not specific for any NDD but increases the risk of them all. Accordingly, her study does not account for the dramatic increase. Although increased clinical skill/knowledge has clearly led to greater recognition of ASD, I was not impressed that she hadn't considered the environmental impact of the virtual digital world on the neurodevelopment of attention and empathy. Other speakers commented on other big changes in our world e.g. the decline of infectious disease and the rise of immunological disorders like asthma. What is the influence of the epidemic of obesity on epigenetics and how does the MicroBiome interact?



In considering the mental health of people with ID, Prof Bruce Tonge recommended that the NDIS should include providing support to enable all to get an annual health check to improve the lack of equity of access. Although more genetic causes of ID are being identified, other predictors of mental health in ID include childhood disturbance, communication problems, lack of social networks, family functioning with disruption causing externalising behaviours and over protection causing anxiety, parental mental health, socio economic status, life events, accommodation and employment.

David Oppenheim from Haifa University presented his research on Mindful Parenting in ASD. While parenting does not cause ASD, the quality of parenting can have significant effect on the outcome and openness of a child with ASD. So often the diagnosis and burden of care overwhelms a mother's capacity such that she loses her mindful parenting style. His team did video assessments of mother and child interaction. Mindful or insightful parenting: 'the capacity to see and feel things from the child's point of view' keeps a mother open to new information and practical approaches and greater anticipatory insight for their child, rather than an emotionality. Only a third of mothers showed this level of acceptance and mindful parenting, which was not associated with the level of ASD functioning, was associated with a secure attachment in the child in 80%. However only 20% of children with ASD had a secure attachment. In a mainstream population attachment disorders are uncommon, although in deprived or abused populations it increases to 40%. He also found parent training intervention for behaviour problems could help a proportion of parents regain their mindful parenting style. Others have shown parent child interaction therapy (PCIT) can improve a parent's mindfulness. His presentation makes clear that both the quality of parenting and attachment is of major importance in ASD and may well provide an early factor in the genesis of emotional and behavioural problems for which there could be intervention.

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Sally Anne Cooper from Glasgow chaired a session on the DSM5 and DM-ID2 diagnostic manuals. The DSM5 diagnoses considers the influence of development, age, culture and gender on diagnosis but not ID, which is why the DM-ID needed renewal. Developmental perspective does consider children and adolescents and has a special section on severe and profound ID leading to limitations and needing adaptions. GAF has been changed for the WHO-DAS for assessing disability. It was encouraging to see UK and EU clinicians collaborating with the USA on the development of the diagnostic manuals, even if there is no funding available to look at diagnostic reliability and differences across the Atlantic. When should diagnoses be considered dimensionally rather than categorically?

Robert Pary presented on bipolar in ID. Levels of evidence remain low. Increased energy is a new primary symptom. Early presentation of bipolar diagnosis has gone up x40 in young people in the last 10 years. Disruptive Mood Dysregulation Disorder (DMDD) is hoped to be a better description of pre-pubertal mood problems which is not episodic like bipolar. Bipolar requires grandiosity for at least a week to distinguish it from DMDD in which mood changes are shorter.

Jane McCarthy presented on Trauma and Stressor related disorders, which now includes the attachment disorders of Reactive Attachment Disorder and Disinhibited Social Engagement Disorder, as well as PTSD. 42% of those with borderline IQ have an attachment disorder. By new definitions Adjustment Disorders resolve in 6 months and is found in 1% of those with mild ID and 2% in Moderate and Profound ID. It is underdiagnosed and suggested by behavioural change, although it is often difficult to identify stressors in ID and often has overlapping symptoms of inattention, impulsivity and hyperactivity. Those with severe ID may have more complex presentations.

Kieron O'Malley in his new book of FASD (Nova: New York; 2016) provides a interesting integration of comorbid psychiatric disorders in NDDs and has drawn attention to the recognition of Disorders of Arousal (in the Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood-Revised (DC: 0-3R)) which occur in infancy and in NDDs such as fetal alcohol spectrum disorders (FASD). Although FASD has not made it into DSM5, the appendix includes, under "Conditions in Need of Further Study", a new disorder of Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE) which includes potential dimensions of: physical characteristics, Disorders of Arousal (including sleep and autonomic arousal), NDDs, and cognitive and executive function problems.

Jacob Burack from McGill University, who presented on Zigler's developmental models in Capetown IASSID, presented on the importance of seeing ability and disturbance in a developmental context. He presented a paper examining the development of attentional cognitive skills in children with an intellectual disability compared to children matched for developmental age which showed no deficit, upholding Zigler's theory of developmental sequences.

The controversy this evoked was extra-ordinary. 10 academics refused to review the article for publication, as it presented a challenge to the field of research in ID, which generally uses age and developmentally normal controls. Evidence demonstrating the importance of developmentally matched controls risks invalidating so much research in ID. They complain that a developmental approach invites too much complexity. Accordingly, most currently funded researchers fail to take account of this universal and humanistic framework which includes a social, emotional and physiological 'whole person', and which underlies every clinician's approach to understanding their clientele. Such an approach to theory and methodology can lead to major advancements in knowledge about the development of persons with ID and the intrinsic links across behaviour, brain, genes and environment. His experience revealed a deep division in methodology between those that consider developmental context, and those that don't.

Helen Appleton from Giants Steps presented the framework for her research into anxiety in ASD/ID based on a dynamic model, proposed by Bartak et al in 2006, of tiers of anxiety from primary to quaternary.

1. due to deficits in processing information,
2. Ritualistic behaviour, poor sensory integration, obstacles to communication,
3. Internalising and externalising behaviours and
4. Psychiatric and personality disorders.

The implication is that all levels need considering, but the highest tier needs treatment in order to access the

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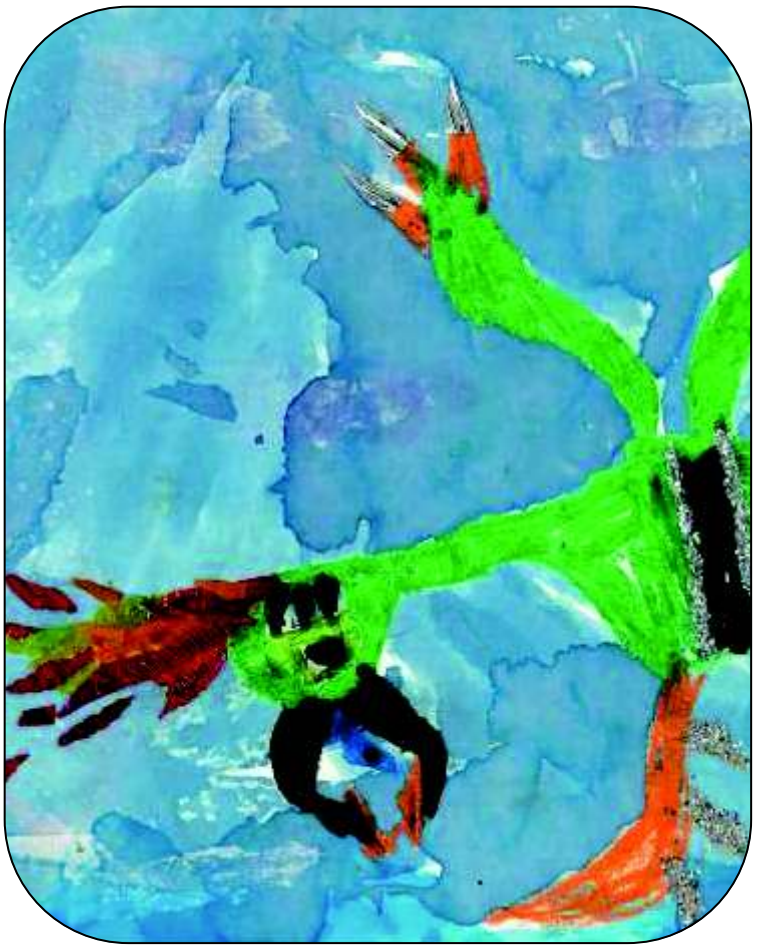
issues of a lower tier. Her colleague Andrew Frakes described a pro-active audit tool for assessing challenging behaviour in ASD/ID by assessing the response to well-known strategies, rather than waiting for the results of an applied behavioural analysis. In the context of skilled teachers, this approach was a much quicker approach to providing intervention.

Flynn did a literature review of psychological and pharmacological intervention in severe and profound ID and using reliable measures of disturbance and outcome and found only 6 papers! This suggests a real need for even single case reports on the value of intervention in severe/profound ID!

Bob Cummins from Deakin University gave a powerful plenary on Quality of Life: 'the Essential Resources for a happy life'. He has a huge database on QOL using his Personal Well-being Index (PWI). Short-term well-being is an emotion, but long-term well-being is a mood that is very stable and with a strong genetic basis for where you lie on the normative centile spectrum between 72-90% (mean 76.7). Those at 90th percentile are somewhat high and irritating, those at 72 are more introspective and show less affect. It is a "normally positive state of mind" that involves everything in our lives. His research has included those with (mild) ID, who generally do similarly well to others. The PWI is underpinned by the well-described 7 dimensions: adequate standard of living and health, intimate relationships, achieving in life, safety, community connectedness and future security. Multiple regression reveals 'the golden triangle of happiness': the three most important factors of: sufficient money (those with disability need a bit more because of their needs), an intimate relationship, and achieving something each day. An intimate relationship is having someone you can winge to!

The other factor is internal reserves or resilience and the capacity to find meaning. His illustration: when you drop your coffee cup in the morning and think how stupid you are, it is the capacity to perspective take and say to yourself that despite that, you still have some good qualities. PWI has data from 12 years old till old age. Alice Schiffers shows that family quality of life has similar domains, where support from others are important in maintaining a positive mood/PWI. Families also rely on trust and reciprocity which can vary considerably. Accordingly, maternal depression can influence everyone in the household. PWI slowly goes down through high school as schools do not focus on personal well-being but focus on exam performance, which in a lifetime perspective, has little benefit to PWI. Getting a job and finding an intimate relationship improves PWI; it goes down with children and a mortgage but improves in the over 55s and remains pretty stable. Bullying and discrimination is harmful to PWI. Depression and mental health problems directly affects the homeostasis of PWI or resilience. Politics should be about the greatest well-being for the greatest number. Curiously economists have realised that there is more to life than gross national product but their approach to quality of life is simplistic. Health-related quality of life is equally invalid: that quality of life is related to one particular symptom.

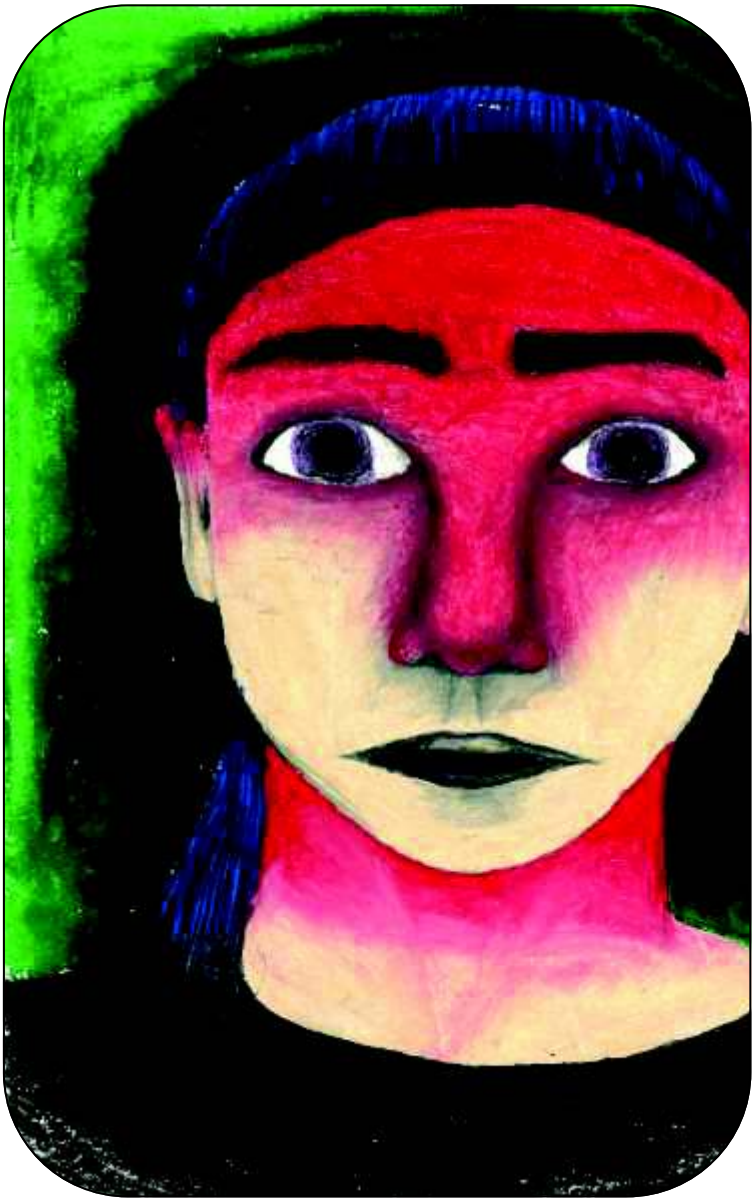
Chris Oliver from the Cerebra Institute in Birmingham gave a masterful lecture illustrating the multiplicity of aetiological factors can cause disturbance. Some of the examples include: physical difference such as different sleep architecture or causes of pain, temperamental difference, social attachment difference or cognitive difference. For example;



Pain: SIB in Cornelia de Lange's Syndrome (CdL) is often caused by gastro-oesophagitis. Similarly In Tuberose Sclerosis SIB is caused by pain especially from flank pain from kidney tubers. He recommends the Face, Legs, Activity, Cry, Consolability scale or FLACC scale (http://prc.coh.org/PainNOA/Flacc_Tool.pdf) for eliciting pain.

Social Attention and Preference: Angelmans is seen as a happy disposition with laughter and sociability but underlying this they have a strong drive for attention. This the drive for attention also leads to aggression when attention is withdrawn such as by turning away, leading to hair pulling and grabbing to greater levels than in other conditions such as Cri du Chat or CdL. Children with Smith Magenis Syndrome are found to have a strong attachment to their primary care giver. At school they tend to attach to one teacher. Experimentally when exposed to an unfamiliar care giver, they continually turned to their mother, in a way not seen in Down Syndrome. It was concluded that they have an excessive attachment to their mother, which causes considerable stress to their mother (on top of being awake at night with their inverted circadian sleep cycle). They may also have high sociability but low social cognition leading to problems in their teens, because they can't read social cues.

Cognitive Difference/Executive function: Prader Willi Syndrome get stressed with demands to switch attention, using executive function testing (EF), which was then correlated with increased repetitive questioning and need for routine. fMRI found related to reduced activity of the fronto-parietal tract compared with typically developing young people, explaining why they have to work harder on the EF task. In effect, carers seeing their behaviour as stubborn and obstinate was pejorative, as they couldn't switch task, not that they wouldn't! Interestingly, whereas PWS have temper tantrums with change (after which they are remorseful), Fra X become anxious. Every year his research group



add new observation to help understand individual differences from their study of syndrome specific clinical features. Each observation raises questions as to whether such phenomena may also apply in certain clinical cases without a gene specific phenotype.

At the end of such a diverse array of presentations, I was forced to conclude that despite different approaches to deconstructing our understanding of emotions and behaviour, the syndromes of psychiatric disorder remain resilient constructs of a different type or order, which are important to study, diagnose and to treat: psychiatric treatment is still an important branch of medicine and recognising their importance in people with intellectual disability remains an important discipline that warrants continued development and investment.

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