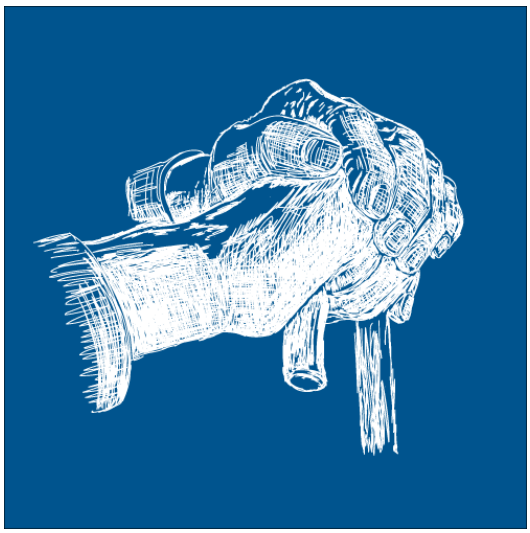
The Old Age Psychiatrist

Issue 82, January 2022

Old Age Psychiatry Faculty Newsletter



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In this issue

Update from the Editorial Team

by
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How time flies – it's nearly the end of 2021 and the January 2022 newsletter is due. Hope you are all keeping safe and well in this new world of beta, delta and omicron….. The newsletter as always has a variety of updates and articles and hope you enjoy reading about the great work Old Age Psychiatrists and other multidisciplinary colleagues do.

The Chair's report highlights all the current relevant issues.

Dr Amanda Thompsell, the National Specialty Advisor (NSA) for Older People's Mental Health (OPMH) at NHS England/NHS Improvement as always provides an interesting and informative update on time to grasp the nettle.

This edition contains three very interesting essays – winners of the National Old Age Trainee Essay prize. All three submissions are interesting and well written.

If you are interested in legal aspects Dr Curtice and colleagues writes on COVID 19 and vaccines and validity of advance decisions in Jehovah's Witness – both make interesting read.

This edition contains our usual Cochrane corner and research update but read also about the Triage as a barrier or tool for integrated care.

Finally this time we have an article on the RCPsych Leadership programme – higher trainees might want to explore this option in future.

Our new Trainee Editor Dr Catrin Thomas, Higher Specialty Trainee is coordinating the Essay competition this year. The title for this year's essay competition is: The Media: Friend or Foe to Old Age Psychiatry. The last date for submission is 28th January 2022. Please encourage multidisciplinary colleagues and trainees to submit.

The next newsletter is May 2022 so the last date for submission of articles is 31st March 2022.

As always let us know what you think of the newsletter, and feel free to email me on drsharmib@gmail.com with ideas, suggestions and of course articles for the future newsletter. Have a peaceful festive period.

View from the Chair

by
Dr M S Krishnan (Krish)

Dear colleague

Hope you are all keeping well and starting to get ready for the festive season.

Thank you all for continuing to deliver excellent services in your local older people's mental health services. We continue to tackle the waiting list of patients who need assessments in memory services and manage workload in our other community and inpatient services.

There has been continued pressure on entire workforce and it is important that we promote support to our colleagues and also look after our own wellbeing. We had a presentation from our Psychiatrists Support service team at our recent executive committee meeting. Please signpost colleagues about this service. This is a free, confidential, and rapid peer support via telephone for colleagues.

https://www.rcpsych.ac.uk/members/supporting-you/psychiatrists-support-service

We had our recent faculty executive committee meeting in November. I thanked the faculty exec members who will be completing their term of office next year.

There will be opportunities for our members to contribute to our faculty as executive committee members. Election will be early next year. Nomination forms are due to be circulated with deadline to submit on 24 January.

We also had feedback from our chairs from devolved nations at the executive committee meeting. In Scotland, work has started on SIGN Dementia guidelines, which will be an excellent resource. We welcomed the new Scottish faculty chair Dr Vivek Pattan. In Wales, Dr Ivenso led a successful conference on early diagnosis. We would like to thank the Welsh chair Dr Ivenso who will be completing her tenure. Our Northern Ireland faculty has been engaging in activities to improve recruitment of both consultant and trainees. There have been 4 new higher trainees recruited with new initiatives.

We had a joint webinar on 8th of September with RCGP, the recording is available at our faculty webpage for those who could not attend.

Old age psychiatry faculty news | Royal College of Psychiatrists (rcpsych.ac.uk)

Our Vice Chair Josie collaborated with our Liaison faculty to run an informal network webinar. We had excellent response and participation from our members and other colleagues. It was a true inter-professional educational event. The recording is available for those who could not attend.

Our faculty trainees conference was held 10 December 2021. Thanks to our trainee reps Dr Manny Bhamra and Dr Orima Kamalu who had put up a fantastic program. Over 180 delegates attended the online conference. Our thanks to Manny and Orima for all their contributions and wish them well in their career. I am delighted to welcome our new trainee Reps Dr Funmi Deinde and Dr Liz Robertson who joined us briefly at the conference.

We had three excellent oral presentations from the trainee abstracts for the poster submission - a higher trainee in Malta, a core trainee, and a foundation doctor. All were excellent.

The picture in this article was taken last week at our refurbished college building. It was lovely to be back at college after nearly two years.

I had a brief informal chat with our Dean and Subodh is keen to run one of Dean's grad rounds with our faculty.

Dr Mohan Bhatt our Academic secretary is busy planning our next annual conference which will be held virtually. Please mark the dates for your diary 24 & 25 March 2022. Its open for booking now.

Please continue to engage with our faculty twitter page @RcpsychOldAge.

Hope you can take some time off during the festive season. I wish you all a happy 2022. Look forward to meeting some of you face to face at least in the New Year.

Krish

Chair of the Faculty of Old Age Psychiatry
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Time to grasp the nettle on behalf of older people

by
Dr Amanda Thompsell, National Specialty Advisor, Older People's Mental Health
Amanda.thompsell@nhs.net

COVID has affected us in all sorts of ways. We know this from our daily lives but to see how older people have fared I can commend Age UK's report (report ID204712). This highlights the devastating impact COVID has had on our seniors. Its focus in particular on health inequalities makes it well worth reading and sharing with colleagues.

Tackling the health inequalities experienced by older people is a long struggle but look carefully enough and there is a silver thread running through the Mental Health Long Term Plan that allows for this. The last few months have been, and the next year will be, important to trying to turn this into practical outcomes for those on the ground.

Investment Opportunities

There are various funding streams available to services for older adults (as well as working age adults) for the different elements of the mental health plan but it has been increasingly obvious that in some cases old age clinicians have been unaware of them, or have lacked the data needed to substantiate a claim based on local needs. Any local funding spend will need to be based on the needs of the local population and the current capacity to meet that demand so there is a clear need for this data.

To help with this NHS England and NHS Improvement (NHSE&I) has done two things.

First we have put together a list showing the various sources of funding across the various workstreams within the NHS Long-Term Plan, what this is available for and how this can be accessed. You can access this list via this link on the FutureNHS Collaboration Platform.

Second, to help you get the necessary data for older adults there are several dashboards for you to use (some being newer than others). The dashboards are all accessible via the FutureNHS Collaboration platform on the page for NHSE&I's National Adult and Older Adult Mental Health Programme (I have included links below which work for logged-in registered users of the platform). The dashboards provide invaluable information broken down at regional, CCG, ICS and provider level (wherever possible). The extent of the variation between areas is significant so the detail is worth studying.

The key dashboards (and links to them) include:

The Urgent and Emergency Mental Health Dashboard. This can be filtered by age and when you do so it provides interesting data about the numbers of older adults accessing routine and urgent services in each area.

The Acute Dashboard. This can be split by bed type, specifically acute older adult mental health care and includes such information as where the person was admitted from, length of stay etc. I know that some colleagues have reported increases in the numbers of people being admitted and length of stay and this data will help you look at this in your area.

The Mental Health Out of Area Placement Dashboard (which is unfortunately labelled the "OAP Dashboard"). By looking at the summary of out of area indicators and scrolling along to percentage of out of area placements by bed type you will be able to see the percentage of older adults in these bed by provider. Once again there is huge variation with some providers having more than 60% of their OAP being older adults.

The Mental Health Act Dashboard. This is in its first iteration. It includes data from the MHSDS on the use of the Mental Health Act (by section type) and by demographics of people detained and much more.

These dashboards provide the data for planning new or enhanced services and can help justify funding for such a plan.

Bids for funding will have the best opportunity for success if they show how the proposal will address any health inequalities and if they have been coproduced.

Education, education, education

Although more money may be available for the NHS generally and Mental Health Services specifically this will be of little use if we do not have appropriately trained staff to run new or enhanced services – a point highlighted in the 2020 National Stocktake of Older Adult Mental Health Services. There is a need to improve the competencies of the workforce to meet the mental health needs of older adults.

In light of this, the National Older People's Mental Health Team at NHSE&I has been working with the Personalised Care Institute (which supports social prescribers, link workers etc.) to produce a webinar on depression and self harm in older adults. This is available at this link (but it can only be accessed after prior registration on the PCI's site, which is easy and free to do).

The team has also been working with NHSE's Ageing Well team who are producing a care learning platform for first year care home staff to include a section on older adult's mental health and dementia. Once the site is up and running, I will let you know the link.

The National Team is also liaising with HEE around a curriculum base for the older adult mental health core competencies.

What gets measured gets done

As I have mentioned above, data is the key to planning and getting the funding for services. Whilst the dashboards mentioned above have taken us a long way, we are not there yet. The National Benchmarking exercise showed up important gaps in the available data on ethnicity. We need to improve this to be able to identify barriers to accessing services. Please play your part in providing this information.

Defining and measuring required outcomes is now *de riguere* for the planning of services and to justify their continued funding. It is important that the right measures are used so as not to disadvantage older adults. The National Team has been actively involved in discussions around outcome measures to help ensure that the outcomes used are relevant for older adults. As a reminder there is also a useful Faculty report on outcome measures on the Faculty website. If you want to share any thoughts on this topic generally please contact me.

There is currently particular interest in the specialist areas of rehabilitation, eating disorders and personality disorders and we are putting together a small working party to articulate what good for older adults might look like in these areas. If you have any views on this please do contact me.

Other resources

There is a webinar on crisis teams for older adults sharing best practice on the National Dementia Programme page of the FutureNHS Collaboration Platform. And the national GIRFT (Getting it right first time) adult crisis and acute care team have a webinar which specifically included older adults.

There is also a 5 minute animation which has been produced by NHSE&I on what is expected from the community mental health transformation which is a useful tool to explain what is going to need to happen.

Finally there is a wonderful 10 minute video on the demographics around the ageing population which can be accessed if you go into the HEE news page using this link and by scrolling down to the video. Although this is not specifically focused on mental health, I would encourage you to share it with anyone who does not share our passion for developing services that can meet the needs of older adults.

Final thoughts

As the COVID pandemic lessens its grip on our day-to-day life, there is an opportunity now to really grasp the opportunities available for older adult's mental health services. I hope some of the thoughts and tools mentioned above will help you make your own contribution to this.

As always, any feedback or comments, please let me know.

The Old Age Psychiatrist: Annual Essay Competition

The title for this year's essay competition is:

The Media: Friend or Foe to Old Age Psychiatry

It is well known that, for better or worse, traditional and social media are powerful influencing tools over public attitudes, perceptions and knowledge. We would love to hear your thoughts and opinions on the media's influence within Old Age Psychiatry including: How does the media portray older people and their mental health needs? What is the media's direct impact on older people's mental health? Does the media influence our practice in Old Age Psychiatry? Should we do more to utilise the power of the media as a tool for change and education?

The Old Age Psychiatrist: Annual Essay Competition

Entries should be no more than 1000 words long. We accept all forms of creative writing including essays, poetry and short stories. We welcome submissions from everyone including Old Age Faculty Members, consultants, trainees and medical students. Please submit your entries to essaycompetition2022@gmail.com by no later than 5pm on Friday 28th January 2022.

Remember to include your name, address and preferred e-mail address when you submit your entry. There is a first place prize of ***£100****, and* ***£50*** *for the runner up! Winners will also have their essays published in the following edition of the Newsletter and will receive a day's free registration at the RCPsych Old Age Faculty Conference in March 2022.*

We are currently organising a fantastic line up of expert judges who will be very excited to read your entries!

Winners of the National Old Age Trainee Essay prize – Core Trainee Essay 1

Weight loss in the older adult: could it be anorexia nervosa?

by

Dr Shannon Hilton, Core Psychiatry Trainee.

Introduction

Anorexia nervosa is a severe psychiatric condition, defined by the ICD-10 as "deliberate weight loss… where a dread of fatness persists as an intrusive, overvalued idea"[1]. Once considered a rare disorder, numerous studies have suggested the incidence of anorexia nervosa is increasing[2,3], with some researchers declaring the incidence as 'epidemic' in Western cultures[2,3]. An important characteristic of anorexia nervosa is the high rate of morbidity and mortality. A meta-analysis settled on a conservative estimate of an annual mortality rate of 5.9%[4], however several other long-term studies have estimated the mortality to be as high as 20%, causes of death including arrhythmias, cardiac failure, suicide, hormonal and electrolyte imbalances amongst others[3,5,6].

Generally, anorexia nervosa is thought of as a disorder of young women, indeed the ICD-10 specifies that "it occurs most commonly in adolescent girls and young women, but adolescent boys and young men may also be affected, as may children approaching puberty and older women up to the menopause"[1]. However, a number of case reports have established that eating disorders can occur de novo in both men and women above the age of 50[7]. Despite this, textbooks, websites and treatment resources frequently assume patients to be young adults or adolescents with references to studying at college or University, and assumptions that primary carers will be parents, with barely a mention of issues specifically pertaining to the older person.

New diagnosis in an older adult may represent a disorder that has evolved insidiously from an earlier age and escaped detection or diagnosis, or may have developed for the first time in later life. Both of these subtypes are of concern, as anorexia nervosa has a high mortality in the older population[8], likely due to reduced physiological reserve, comorbid physical and psychiatric conditions and difficulties establishing diagnosis. The relatively low frequency of new diagnosis in older adults may be due to misdiagnosis or diagnostic overshadowing, possibly due to a lack of awareness or accessibility of practitioners specialised in eating disorders.

Prevalence of anorexia nervosa in later life

It has been widely established that symptoms of eating disorders do occur in mid- and late-life. Many studies have been carried out, often looking at the prevalence of eating disorder symptoms in community samples. A cross-sectional study of elderly Canadian women reported that symptoms of disordered eating were present in 2.6% of women aged 50–64 years, and in 1.8% of women aged 65 years or older[9].

In an investigation of eating disorders in elderly underweight outpatient males, a minority (11–19%) were found to have abnormal eating attitudes and body image[10]. Whilst the most common symptom was inappropriate self-control around food (60%), the men less frequently demonstrated unsuitable eating attitudes (26%) or distorted body image (3–52%), thus suggesting abnormal eating patterns and body image do occur in elderly men, but present in a different pattern to that seen in typical anorexia nervosa[10]. Indeed, after the age of 45, new presentations are more common in men as the female: male ratio rises from 9:1 to 8:2[3].

A literature review[8] of 48 published case studies of adults aged 50 and above with eating disorders found the majority (81%) of cases had anorexia nervosa and 10% had bulimia nervosa. Late onset eating disorders were more common (69%) than early onset. Comorbid psychiatric conditions existed in 60% of cases, most commonly major depression. The mean age of adults included in this study was 68.6 years (range 50–94), and the majority (88%) of cases were female.

In contrast, one London-based study used a large eating disorders outpatient caseload to determine whether current patients aged 50 or above had a lifelong

or late onset illness. 32 patients aged over 50 at the time of the study were identified; all of whom had an age of onset less than 25, with a mean age of first presentation to psychiatric services aged 31 (interestingly, all 32 patients presented to services at least 10 years after onset)[7]. The authors noted a high prevalence of psychiatric comorbidity in this group, most commonly depression (46%), followed by anxiety disorders (31%), alcohol dependency syndrome (19%), and personality disorder (19%)[7].

Weight loss as a marker of ill health in older adults

Weight loss associated with aging is not uncommon, yet correlates with increased morbidity and mortality[11]. For example, one study of institutionalised elderly patients showed that those who lost >5% of their body weight in one month were four times more likely to die within one year[12].

Anorexia (defined as reduced appetite and/or food intake) is a major contributing factor to mortality and morbidity in the geriatric population[11]. Compared with younger patients, weight loss in the elderly is much more likely to be unintentional and secondary to another disease process, such as depression, cancer, cardiac disease or gastrointestinal disease[13].

Unintentional weight loss may be caused by medication side-effects such as nausea and vomiting, dysphagia, loss of appetite or changes to sense of taste and smell[13]. Polypharmacy is known to interfere with taste sensation and cause anorexia[14,15]; sedatives and other drugs may interfere with cognition, alertness and the ability to eat[16]. Whilst some selective serotonin reuptake inhibitors are known to have an anorectic effect, reduction in the dosage of psychotropic medication may worsen anxiety or depression, also leading to weight loss[13,17].

For some, anorexia in the older adult may be due to the accumulation of health impairments in multiple systems combining to increase vulnerability to internal and/or external stressors[11].

Normal endocrine changes that occur in later life also predispose older persons to weight loss, as the level of cholecystokinin, a satiating hormone, increases in the circulation. This can lead to a change in food intake patterns (e.g. eating smaller quantities and less frequently) some of which can be explained by reduced physical activity in advancing years[18].

Diminished food intake may also occur as the sense of smell and taste decreases with age, thus making food less enjoyable and typically resulting in a less varied and blander diet[11]. The number of taste buds decreases during normal aging, a process which can be exacerbated by disease, medications, smoking, and some environmental exposures[11,19,20].

Functional impairments in activities of daily living are related to reduced food intake and loss of appetite. Impairments in the ability to purchase and prepare food, and feed oneself are relevant risk factors for anorexia of aging[11]. Poor dentition and ill-fitting dentures, may limit the type and quantity of food consumed through impairment of normal bite and chewing. Chewing problems can lead to poor nutritional status and is associated with lower intake of specific nutrients, including fibers, vitamins, calcium, and proteins, and with a higher intake of fats and cholesterol[11,21].

All patients complaining of weight loss, whether presenting to the eating disorder clinic, emergency department or general practitioner, should be investigated thoroughly for common causes such as cancer, gut pathology and depression. A loss of approximately 5 to 10 percent of body weight in the previous year may indicate presence of disease in an elderly patient and should not be considered a normal part of the aging process[13].

A reasonable battery of tests for any older patient presenting with weight loss would include a full set of blood tests including thyroid function, vitamin deficiencies and coeliac screen, faecal occult blood test and urinalysis, basic psychiatric evaluation considering depression and cognitive impairment, as well as considering whether an upper endoscopy may be warranted[15,22]. Despite gold standard test batteries, in up to one quarter of patients no cause may be found for unintentional weight loss[13,23,24].

In the psychiatric clinic, weight loss in older age is most classically associated with depression[25]. Studies have found scores on depression scales to be positively correlated with weight loss in geriatric outpatient clinics[25]. Among those diagnosed with depression, older adults suffer more severe appetite and weight loss than their younger counterparts[11]. Some studies have found comorbid depression in up to one third of nursing home residents with unintentional weight loss[17].

Individuals with cognitive impairment may also demonstrate a loss of appetite and reduced food intake, especially in the latter stages of the condition[8]. An older adult may present on 'hunger strike' as an act of protest, expression of anger at aging and loss of independence or as an act of self-harm or suicide, contrasting with anorexia nervosa where body image disturbance is seen and there is an over-valued ideal of thinness[26].

A suspicion of an eating disorder should be raised in patients of any age (including older people) when weight loss is associated with phobia of weight gain, induced vomiting or drive for thinness and should prompt urgent and thorough specialist psychiatric assessment[27].

Assessing the older patient for anorexia nervosa

Recognition of an eating disorder can be difficult in a geriatric patient with multiple comorbidities, especially if involved professionals are unfamiliar with the diagnostic framework. As discussed previously, weight loss in the elderly is much more likely to be assumed to be due to an undiagnosed medical illness, than in younger patients[8].

The symptomatology of eating disorders in the elderly is the same as that for younger patients, other than the absence of menstruation. The core features for a diagnosis of anorexia nervosa, as listed in the DSM-V are 'restriction of energy intake relative to needs leading to a significantly low body weight, an intense fear of weight gain and over-valuation of weight or shape, or disturbance in the way one's body weight or shape is perceived'[28].

It is important to note that a serious eating disorder may still be present, even if not all criteria are met (including low BMI); related pathologies such as bulimia nervosa, binge eating disorder and ARFID (avoidant-restrictive food intake disorder) are not discussed here. Indeed, a study in a convenience sample of more than 1800 females aged 50 and over, found disordered eating attitudes and behaviours more frequently in the group with a BMI over 25[29]. Some patients come to the attention of professionals having lost a significant amount of weight, but remaining a healthy BMI (18.5-25); a 'normal' weight should not preclude treatment or diagnosis. The diagnosis of 'atypical anorexia nervosa' can be given if there is clear over-valuation of weight or shape, restriction of oral intake or excessive exercise and a drive for thinness, despite not being underweight[28].

At assessment, a timeline should be established indicating the speed of weight loss, noting any concurrent physical or psychiatric symptoms and any significant life events, such as bereavement, relationship loss or changes or trauma. All patients should be screened for a past history of disordered eating in adolescence and early adulthood; this may not have been previously diagnosed or recognised by the patient as such.

Other psychiatric disorders such as depression, anxiety, psychosis and cognitive disorders may resemble eating disorders in the elderly. A lack of the classic cognitive distortions (a desire to be thinner, preoccupation with weight or body image distortion) will distinguish other psychiatric complaints from true eating disorders[8]. Both patients with anorexia nervosa and depression may complain of low energy, anhedonia, poor concentration and memory difficulties. However, features of depression such as insomnia are not classically present in the eating disordered patient and body image disturbance reaching a delusional intensity (e.g. Cotard's delusion) should raise suspicion of a primary psychotic process[26]. Anxiety disorders, obsessive compulsive disorder, and social phobias have also been associated with eating disorders[30,31,32].

Given the high mortality associated with an eating disorder in the elderly, once the diagnosis is suspected, a thorough assessment should be made and consideration for referral to local specialist services for prompt and aggressive treatment[8].

Predisposing factors and common features

As previously discussed, there is currently no difference in diagnostic criteria when considering eating disorders across the lifespan, other than discounting the absence of menorrhoea in a post-menopausal female.

Many case studies give descriptions of disordered eating which appear similar to typical presentations in younger patients[10]. However, other atypical cases have lead authors to suggest there may be different psychological processes that predispose one to developing eating disorders in later life. For some, eating disorders may represent a method of protest by drawing attention to unhappiness that is difficult to express, or simply to relieve a sense of dysphoria[33,34]. Other researchers have suggested that biological mechanisms that lead to loss of appetite (such as those discussed earlier) may usher in eating pathology[8].

Self-starvation, excessive exercising or binge/purge behaviours can become entrenched in any age group as corrupt mechanisms to reduce distress generated by psychodynamic conflicts, mood disorders or interpersonal distress[34]. Proposed psychodynamic mechanisms include narcissistic preoccupation with the body; devaluation of older women; envy of younger generations; need for control, and unresolved loss[35].

Eating disorders in adolescence are frequently linked to crises related to reaching sexual maturation and adulthood. Likewise, women in middle or later life may rely on an eating disorder to resist the natural transition to the next stage of adult development[35]. Erikson[36] described development as a lifelong process requiring successful navigation of conflicts at each stage; the transition from middle to late life is marked by reflection on a life well-lived, participation in life-affirming activities and desire to nurture younger generations. This may require healthy adjustment to, for example, children leaving home, becoming a grandparent, changing or leaving career and marital transformation (including bereavement and divorce).

One must accept, or even mourn, what is no longer theirs – youth and a youthful body. It may be that in late onset eating disorders, resistance to the mourning process halts healthy development as the individual remains preoccupied with a desire to attain an idealised, stereotyped notion of youth, characterised by a slender body and smooth face. Ranking external markers of success and attractiveness above internal markers (such as generativity and wisdom) is risky as one invests high levels of psychological energy into avoiding the inevitable natural process of aging and eventual death[35].

Western society dictates that a woman's value is tied to physical attributes (a message repeated across all forms of modern media) with little to envy or desire by growing older; thus as women age they become increasingly devalued by society. Competitiveness is rife, with an expectation of perfectionism in all areas of life requiring significant ego strength to challenge such cultural norms[35]. An early marker of sub-clinical eating pathology may be an over involvement in the body at mid-life at the expense of other activities and interests[35].

A study examined the relationship between apprehension about aging and a drive for thinness and body dissatisfaction in a group of men and women attending dermatology clinics for complaints related to aging skin. A direct correlation was

found between concerns with the effect of aging on appearance and the level of preoccupation with weight, dieting and exercise[37]. In this study, the group who received 24 weeks of topical retinoic acid (known to increase appearance of skin plumpness, reduce fine lines and dark spots) demonstrated a post-study improvement in scores on the drive for thinness and body dissatisfaction elements of the EDE-Q disordered eating questionnaire[37]. A separate study reported that body dissatisfaction and importance of body shape did not differ across the lifespan, somewhat in contrast to presumptions that older people lose interest in their physicality, femininity/masculinity or sexuality[38].

A literature review of all published case studies identified widowhood and bereavement, marriage-related difficulties and medical illnesses as the most common stressful events heralding the onset of eating disorder symptoms, however this represents a small sample of less than 50 cases[8]. Common features of aging such as social withdrawal, shrunken circle of interest and increased preoccupation with food and mealtimes may predispose an individual to an eating disorder[8]. A period of mourning may be required, not just for bereavement of others, but aspects of the self that have been lost through aging such as autonomy, social roles and youth itself, is essential to enable the person to move on and realise healthy psychological maturity[35].

The painful acceptance of one's own limited time is contrasted against others' lives who seem to be just beginning. At times fantasies about what one once was, or could have been, are projected into children or younger adults[35]. Whilst this projection is often well-meaning (e.g. encouraging hobbies or curricular pursuits), it may be perpetuated by competition or envy. Instead of reaping the benefits of the next life stage, women may remain stagnant, preoccupied with concerns of younger women[35].

Another proposed causal mechanism of eating disorders in the elderly is the need for control. Aging adults increasingly lose control over their bodies (through deterioration with age and illness), over others (as social roles in the workplace or family are lost or redefined) and their future (as goals and outcomes become curtailed and increasingly dictated by others). A powerful method for gaining control through therapy is to examine what was never under one's control in the first place i.e. the aging process and ultimately death[35].

Anankastic traits are highly comorbid with eating disorders; it is likely that in susceptible individuals eating disorders may function as a control mechanism to regain power in their lives[33,39]. Overly controlled personalities are more vulnerable to remember and ruminate upon childhood neglect and emotional distress[34]. A seminal case series noted the predominance of memories of traumatic experiences in elderly eating disordered patients: one patient recounted being teased as a child for her weight, another described emotional trauma from her husband who denied breast reduction surgery intended to alleviate back pain[34]. Often the traumatic event occurred years before symptoms, suggesting latent psychopathology may manifest later in overt eating disorder.

One review found that 60% of elderly people with an eating disorder had a comorbid psychiatric illness, most commonly major depression[8]. Major depression has been shown to be 2.4 to 4 times more likely in individuals with anorexia (at any age) than in controls[40]. Eating disorder increases risk of major depressive disorder, especially in individuals' suffering from bulimia nervosa (comorbidity estimated 31-50%)[40]. However some caution is advised in applying these findings as many studies do not include older adults[41].

A recent meta-analysis of longitudinal studies, found eating pathologies and depression are concurrent risk factors for each other, however this study was not specific to older adults[32,42]. Prior to this meta-analysis, various studies have found uni-directional relationships and postulated their mechanism: eating disorder may induce depression via shame and guilt generated from the distress of 'failing' to achieve the physical ideal (experienced clinically as the 'never [thin] enough' phenomena)[42]. It is also possible that the direct effects of constant starvation on the brain are enough in themselves to generate mood difficulties[42].

Alternatively, when considering whether depression predicts eating disorders, it has been suggested that binge-eating symptoms develop as a tool to regulate affect in the depressed individual via distraction or comfort. Other symptoms (e.g. restriction or purging) may also regulate affect by reducing negative feelings, or that these behaviours serve an emotionally cathartic purpose[43].

Of course, these hypotheses are not mutually exclusive and others have claimed that a bi-directional relationship exists[42]. It is also possible that eating pathologies and depression share common risk factors, which may be genetic, psychological and environmental.

Mortality

Anorexia nervosa is frequently cited as the psychiatric condition with the highest mortality; indeed, of the 48 cases of older adults published at the time of Lapid's literature review, approximately 20% of the patients had died due to the eating disorder or related complications including cachexia, pneumonia and cardiac failure[8].

Perhaps the most unexpected finding is the age distribution of the anorexia nervosa deaths seen. Given the predominance of anorexia nervosa onset in adolescence or early adulthood, one might expect that the majority of deaths would be among the young. However, one study found for women the median age of death to be 69 years, and for men 80 years, suggesting that anorexia nervosa contributes to death across the age span and may, in fact, be more closely related to death in the elderly, rather than among adolescents and young adults. The distribution of age at death for women shows a bimodality, with a peak at age 35 followed by an ascending rate of mortality with increasing age. The most common complication is bowel dysfunction; the most disabling is pain from multiple osteoporotic fractures[3]. For males, only the latter trend, the increased risk amongst the older population, is apparent. Furthermore, at least as listed on death certificates in the USA, deaths occurring below the age of 45 involving anorexia nervosa encompass only 21.4% of the total number of anorexia nervosa-related deaths, with the bulk of the deaths occurring in the latter half of life (78.6%). However, it should be noted that these patterns are for frequency, rather than relative risk; the highest risk of death by anorexia nervosa for females is in the two decades spanning the 15± 34 age range, where it is 64.3 per 100,000 deaths[3].

Recommendations

Truly late-life onset eating disorders do exist and occur in the elderly. It is likely they are under-recognised and victim to diagnostic overshadowing from physical health or psychiatric pathologies. Standard assessments may fail to illuminate core cognitive symptoms of anorexia nervosa.

It appears that late-life onset eating disorders are commonly complicated by other psychiatric diagnoses. Therefore, it seems prudent to develop successful management strategies to treat both the eating disorder and comorbid psychiatric disorder, whilst recognising the different psychological stressors in the older adult.

It is likely a combination of pharmacological, psychological and behavioural intervention is indicated in many[8]. In one literature review, management with a combination of behavioural and pharmacologic interventions was most successful, although only 42% of patients were treated successfully (defined as reduced symptoms or maintained weight restoration)[8]. As previously discussed, mortality in this group was high (21%) secondary to the eating disorder and its complications[8].

Clinicians experienced in the area have noted that symptoms in the older adult are often denied or minimised, a feature common to eating disorders across the lifespan. This is often the result of intense shame and guilt; often symptoms have been hidden from others for many months, if not years. Experienced therapists will be familiar with meeting resistance from patients who struggle to give up their disordered eating, despite clear evidence that the eating disorder is health-, if not life-, threatening as it represents a defence against something the patient fears will be even worse[35].

Treatment for the older adult will be different to younger patients, for example rather than parents' involvement: it will be spouses or children who will be involved in care; older adults are more likely to have a sparse social support system compared to their younger counterparts; older individuals frequently have coexistent medical illnesses that may cloud the clinical picture of an eating disorder. Whilst joined up multi-disciplinary working is our recommended gold standard, eating disorder services tend to be regionalised and may not share the same information systems as local physical health hospitals and GP surgeries - it is much less likely that eating disorder services will have a geriatrician or other physical health specialist working within the service. The risks of adverse effects or drug interaction is likely to be increased for an older adult, who is more likely to be taking multiple medications for various medical conditions potentially alongside psychotropic medications to treat the eating disorder and comorbid psychiatric conditions[8]; a geriatrician and pharmacist may be best placed to advise in these cases.

Patients enrolled in qualitative studies have described frustration with the limited healthcare provision for older people with eating disorders. Many of these patients suffered from chronic eating pathology; they described good inpatient services for young 'acute' patients but felt community follow-up for more chronic patients was

lacking. They recognized that older people with eating disorders were in the minority but felt ageist attitudes of staff contributed to this lack of provision. One patient had visited her general practitioner to be told 'you're too old to have an eating disorder'[7].

Common interventions may be inherently ageist or inappropriate, for example CBT may have limited utility in the older person with comorbid cognitive impairment[8]. Patients have described websites as unhelpful, as they focused solely on younger people[7].

The scope of this essay is not to provide a definitive blueprint for how eating disorders or older adult mental health services should operate. It does however aim to raise awareness of an under-recognised condition and ask the reader to reflect on their own practice and that of their service. Further research should be commissioned to answer questions such as: whether training around eating pathologies in older adults should be developed and delivered to stakeholders; whether clinicians routinely ask screening questions for over-valuation of thinness when assessing the older adult with weight loss; whether current psychological and medical treatment are effective in older adults and whether new, specific treatments are required. Services should consider developing pathways to seamlessly blend the expertise of geriatricians, pharmacists, older adults' psychiatrists and eating disorder specialists.

As the population ages and with eating disorder prevalence estimated to increase further, perhaps this is the time to begin answering some of these questions through new, dedicated research.

References available on request.

Essay 2

Psychosis and Grief phenomena in Alzheimer's Disease: exploring the evidence for a distinct phenotype.

by

Dr Sabeera Dar, Foundation Trainee.

There is no hiding that Alzheimer's Disease (AD) can be a devastating diagnosis. Time spent on the old age psychiatric unit has offered insights into how insidiously this condition can warp personality, memory and our sense of self. My interaction with one particular patient illustrates this perfectly:

A case study from the ward

I was rushing into the office when I saw her face shifting, like a sky before a monsoon. Her hair was wrapped in a small black fabric and twisted around the sides into a neat mini turban. She stood anchored by an aura of being forlorn. But her eyes were capacious and knowing. A nightmare was unravelling beneath and there was nothing antipsychotics could do to stop it.

"My husband is dead." She informed me, her voice both firm and fragile. "I was talking to him earlier, shouting upstairs this morning and he's stopped replying. I think he's died up there and no one seems to want to know anything about it," she added.

I tried feebly to reassure her that I had heard nothing about this and that I'd have a look upstairs, but my words were like water, casually slipping off leaves and not a trace of understanding remained. She continued, propelled by panic, "all I want is someone to have a look and tell me what's going on, if he's fallen over or if he's gone. Something awful has happened and I can feel it." She gestured to her chest and her voice cracked as she spoke. I said I was sorry she was going through this but at least she has the staff here and her daughters to support her. Perhaps she'd

like to speak to one of them now, I suggested, thinking a rooting in reality through someone other than me could be a kinder way to shatter the illusion. Her voice hardened, "my daughters, you know nothing of my daughters. M is in jail. She's incarcerated, what can she possibly do for me?" She gazed at me, a slow resignation overcoming her.

For the first time I tried to challenge her delusion. Seeing her like this, I couldn't help it.

"But I saw your daughter yesterday with you?" I offered meekly.

"Well that's not possible. She's behind bars. I'm all alone." she snapped. I resisted the temptation of exploring her psychosis and instead tried to tell her that she had lots of people around her who cared for her. Rejecting my entreaties, she continued down the hallway towards her room, spilling to me how all she wanted was to know what happened to her husband.

Once in her room, she suddenly stood still. Immaculate. Her turquoise blazer embellished with her favourite brooch. Partnered with her smart black skirt, she always dressed as though she was departing, as if in perpetual transit. Closing her eyes, she searched for his voice, yielding nothing. She opened her eyes, returning to this nonsensical purgatory and then perched crestfallen upon her bed. Tilting her anxious face to the ceiling, she yelled, "CHARLES ARE YOU THERE!?" Nothing. Of course, nothing. She shook her head in dismay, "I seem to hear him slightly but I can't be sure - there's just so much noise everywhere." Indeed, outside the seafront gusts were carrying rain, battling with the stamina of the trees.

I thought perhaps some verbal de-escalation could be of benefit here. I told her I'd been upstairs and not seen him, maybe he'd gone away for now, hence why he stopped responding.

"Or he's died. Can you go and check? His full name is Charles Baldwin, I'm certain something bad has happened to him, I just know it."

"Not necessarily." I found myself playing along. "I would go up there myself but I don't know the way. I can't do anything, I just want to know if my husband is dead or not." Her voice now quivering, all her usual poise on the verge of slippage.

She put her head in her hands. Cradling her brain, the same one that was crafting persecutory delusions at full speed, relentlessly barricading her in a fictional grief.

But how fictional was this grief? I stood spectator from the doorframe, thinking here is a woman grieving over her dead husband. In reality, he died years ago. She is cyclically reliving his death, maybe finally coming to terms with it. Or is this merely a figment of her psychosis and nothing more? I wondered if it matters what realm her grief exists in for it to encompass her, for others to empathise and for it to count as a legitimate ache? After all, her brain is responding with emotional turmoil as real as the skin on my hands.

She crouched over, her eyes fixated forwards on a theatre in which she was the only audience. I told her I'd give her some space and that we'd be here if she needed us. "Thanks for talking to me," the words always tumbled out in the same haphazardly innocent way. Her typical close to our conversations, albeit circular, was always of gratitude.

The question of whether or not to dislodge someone's delusions is a precarious one. I like to think we should refrain from it, as we do from violently shaking awake sleepwalkers. Allow the person to feel safe with you and pull delicately at the periphery until they begin to sense their way out. This seldom happens in patients so severely starved of insight. Because it's not like spoiling a spider web of ideas, it's more like reaching into quicksand and feeling the sheer force of their convictions tamper with your own repose. But we gather composure and go on.

<u>Background: why is it important to consider psychosis in Alzheimer's Disease?</u>

This case gives a glimpse into some psychological difficulties endured by those with AD. Though exact genetic mechanisms underlying AD remain elusive, there have been major advancements using gene-mapping.[1] Defining sub-groups of AD (early-onset vs late-onset) has enabled better mapping of culprit variants, like the ε4 haplotype in apolipoprotein E on chromosome 19.[1,2] Whilst we understand more of the highly heritable early onset form type of AD, this constitutes only a minority of cases.[2] The presence of psychotic symptoms in AD is common. In fact, the estimated prevalence stretches from 10-73%, with most studies stating a figure of around 40%.[3] Intriguingly, the presence of psychotic symptoms on a background of AD confers an increased risk of psychosis to affected siblings.[4]

A recent Nature review critically explores the possibility of defining a clinically significant syndrome existing of AD and psychosis (AD+P).[4] The clinical relevance of elucidating this link is clear, given that those who go on to develop psychosis alongside AD face greater cognitive impairment, higher rates of premature institutionalization and higher mortality than AD patients without psychosis.[5] Manifestations of agitation, physical/verbal aggression and anxiety, dominate the picture in this subgroup.[6]

The presence of psychotic symptoms can make managing a loved one's dementia much harder and command the full attention of an ageing population. With global predictions of AD set to reach over 100 million by 2050, AD+P will become an increasingly common cause of psychosis worldwide.[7] Therefore, understanding AD+P is sure to become a public health goal in the coming years.

Moved by the intensity of the patient interaction outlined above, I became eager to further explore the prevalence of psychosis and grief phenomena in Alzheimer's disease. What does it mean for patients, for geneticists and for the global psychiatric community moving forward? At present, the limited knowledge of disease mechanisms behind AD+P represent a major impediment in understanding the syndrome at a clinical level.

In this essay, after outlining AD+P and some of the social and clinical obstacles faced in its diagnosis, I will consider some of the neuroimaging and neuropathological evidence concerning whether AD+P could exist as a unique syndrome. Then I will review recent genetic work on AD+P and explore its links with schizophrenia. Additionally, before concluding, I will briefly consider the reported neurotransmission alterations in this patient cohort and then offer suggestions for future research in this field.

What symptoms distinguish AD+P?

The distinct phenotype of AD+P is neatly defined as the presence of hallucinations and delusions concurring with AD. Usually, we regard disorganised thought processes without delusions and hallucinations as a standard facet of AD. One US study showed that amongst those in nursing homes with dementia and psychosis, nearly two thirds have symptoms that persist over 12 weeks.[3] For outpatients, hallucinations and delusions can persist for over 3 months to a year.[3]

Coping with delusions and bereavement delusions in AD

Delusions are wide and varied in AD, ranging from delusions of infidelity to those of abandonment and persecution. Misidentification delusions are also frequent in AD patients, for example that television images are animate and loved ones have replaced by an exact duplicate, i.e. Capgras syndrome.

In the story above, my patient grapples with intense delusions of grief on a background of AD. Dealing with such delusions can prove jarring as they often resemble some permutation of a previous reality. Grief and the reliving of it, can perhaps be indicative of never really having processed it properly in the first place or simply a fallout of a severe depression, developed in the context of dementia. Such helpless repetition and futile attempt at resolve is compared with the punishment cycle in the Greek myth of Prometheus within this paper looking at bereavement in cognitively impaired adults.[8] Cognitive impairment can interfere with the normal coping tools employed to navigate loss. The Harvard bereavement study state that a crucial component of grieving is the emotional and cognitive acceptance of death which paves the way for forming new connections within the community.[9] Those with dementia may be isolated and struggle to form these vital new connections, rendering them unable to process the unspeakable hurt they have suffered.

Furthermore, the inability to communicate the distress brought on by grief hinders the process of emotional repair. We know that frontal lobe damage compromises episodic memory and warps the processing of affect-laden expression.[10] Brain imaging has not yet shown how those with frontal and temporal lobe damage experience bereavement, but one could speculate that such brain changes modify the experience of grieving. The inaccessibility of treatment modalities like psychotherapy for elderly patients with dementia means working out how to respond effectively is difficult. Both caregivers and clinicians are repeatedly confronted with the dilemma of reality reorientation.[8] Hiding the fact of death, both previous and historical, can be traumatising for staff and patients. Guidelines on how to break such news to someone with AD or even AD+P are scarce, which is unfortunate - given it is such a common occurrence. This is especially relevant for outpatients who have family members looking after them, as such delusional themes about deceased relatives can prove extremely distressing. Nurses and caregivers should be primed on this sensitive topic in order to handle each case

with the required sensitivity, lest patients respond with hostility. Achieving this delicate balance in the community is notably difficult, often leading to carer burnout.

Hallucinations in AD

Recognising hallucinations in elderly patients with dementia presents another complex endeavour. Firstly, they can occur transiently at different times of the day or may even be misconstrued as delirium. The differentiation here is critical in order to rule out any underlying acute pathology or ophthalmological causes like Charles-Bonnet syndrome.[11] There have been several rating scales developed for the purpose of identifying psychosis in AD and these have been deemed to have high inter-reliability. Alongside success seen by the consortium to establish a registry for Alzheimer's disease (CERAD), there remains an undeniable need for significant clinical judgement in assessing for psychosis in AD.[12]

The case for a distinct phenotype (AD+P); what does the literature say?

Let us move on to examine some of the evidence pointing towards AD+P emerging as a distinct phenotype. The concept of state independence demands that psychotic symptoms ought to be present over the course of having AD. A recent review considering studies that lasted 6 months to 5 years confirmed significant persistence of these symptoms with a high recurrence rate of AD+P of 95%. [4, 13] Moving forward we need to interrogate whether psychotic symptoms arise as an epiphenomenon towards the latter stage of illness or whether another unidentified causation is linking deteriorating cognition and psychosis?

Most evidence on the topic suggests that psychotic symptoms are rare in the prodrome of AD.[14] Another important thing to note is that AD+P is not only linked to worse cognitive impairment but also with worse cognitive decline.[15] There has only been a single study assessing cognitive decline prior to psychosis onset and this showed increased cognitive decline preceded by psychosis onset.[15] Thinking about other disorders like schizophrenia and major depression, we know that psychosis is tied up with intrinsic cognitive impairment, suggesting AD+P and excess cognitive burden may share underlying mechanisms.[16]

Having said that, the relationship between cognitive deterioration and psychosis in AD is fraught with red herrings. Well-formed visual hallucinations are a hallmark

feature of Lewy body Dementia (LBD) and delusions are considered an accessory diagnostic aspect. It follows then that the presence of Lewy bodies could be a confounding factor in the association with functional deterioration and AD+P. Currently, antemortem criteria for differentiating LBD from AD in mild illness carries low sensitivity. This means that the clinically labelled AD cohorts that are being included in research trials may well contain some LBD patients. Even if such patients are found in this sample, it is unknown to what extent this impacts the observed effect. Recent data that has been collated using new methods that employ antibodies against alpha-synuclein to detect Lewy bodies.[17] It was found that alpha-synuclein aggregation may be present in up to 50% of cases with neuro-pathologically confirmed AD.[17] Whether psychotic symptoms in AD are caused by smaller areas of LBD has not been examined. However, having areas of Lewy bodies in the presence of neurofibrillary tangles would be classed as AD with comorbid LBD pathology.[18]

Neuroimaging evidence for a distinct phenotype (AD+P)

The clinical implications of AD+P have informed research in neuroimaging attempts to intimately map the psychotic AD phenotype.

The hypofrontality model of AD+P seems to be the most popular amongst current literature, with PET studies showing reduced blood flow and metabolism in the neocortex of AD+P subjects.[19] A study looking at single photon emission computed tomography (SPECT) profiles showed that AD+P cases had lower regional perfusion in bilateral dorsolateral frontal, left anterior cingulate and left ventral striatal regions, along with the left pulvinar and dorsolateral parietal cortex in comparison to the non-psychotic group.[20]

Untangling some neuroanatomy would be of use here. The dorsolateral prefrontal cortex is a segment of the frontal lobe typically associated with selective attention and working memory, whilst the anterior cingulate is implicated in impulse control and empathy. The ventral striatum is a vital part of circuitry involved in decision making and reward-related behaviour. As the largest nucleus of the thalamus, the pulvinar has important connections to the visual cortex. Dysfunction in these areas are changes in keeping with AD+P symptoms. A different review of MRI's on psychosis in AD found greater impairment in right hemisphere brain regions, especially in the frontal and temporal lobes.[21]

The changes mentioned above are generic to all cases of AD+P; other studies have gone a step further. Psychotic symptoms in AD can be classified as either paranoid (persecutory delusions) or misidentification. Whilst the misidentification subtype has been shown to be linked with greater cognitive decline and more frequent deficits in visuo-perceptual functions;[22] the paranoid subtype is associated with greater impairments in working memory.[23] Neuroimaging studies focusing on the misidentification subtype have shown evidence of greater atrophy in the ventral visual stream and the left parahippocampal region as well as in the right middle frontal gyrus, the inferior parietal lobule, and the occipital lobe.[24] This is consistent with the clinical presentation of AD+P as the parahippocampal region plays an imperative role in the retrieval and encoding of memories. On the other hand, the paranoid subtype is not associated with a greater degree of atrophy than that observed in non-psychotic patients.[25] Greater grey matter atrophy in the bilateral parahippocampal gyri has been detected in those who develop delusions over time than those who did not.[26]

Furthermore, a 2019 study looked into whether impairment in a certain domain could predict the onset of psychosis and if the rate of atrophy of specific grey matter could be a distinguishing feature of AD+P profiles.[27] The authors state that there was atrophy in the right ventral and anterior temporal lobe in psychotic than non-psychotic AD patients. In addition, both psychotic and non-psychotic AD patients exhibited greater atrophy in the insula, anterior cingulate cortex, and superior frontal gyrus bilaterally when comparing baseline scans and those taken 2 years later.

Lastly, they mention that the rate at which grey matter declined in the right insula over the time tended to be faster in psychotic than in non-psychotic AD patients. Located deep within the lateral sulcus of the brain, the insula is an intriguing structure and has been shown to play a central role in the onset of delusions in psychiatric patients.[28] Other studies have also hinted at hypoperfusion in the insula modulating the severity of delusions.[29] Damage to the insula may explain the overattributing of importance to the misperceived stimuli.

Such findings corroborate the hypothesis that the inability to verify beliefs partnered with visuo-spatial impairment leads to psychotic symptoms via the loss of attentional control. There is also emerging research hinting that changes seen in frontotemporal atrophy are not consistent between the sexes.[30] These studies

have their limitations including the sample size being restrictive and the challenge of differentiating the subtype of psychosis experienced by patients who are often present with a mixture of both.

Considering the intersection between LBD and AD+P in neuroimaging has proven to be informative. A Norwegian project sought to examine the post-mortem pathological correlates of severe psychotic symptoms in moderate AD and LBD.[31] Participants were followed annually from the time of diagnosis to death. The main finding was the potential link between cerebral amyloid angiopathy (CAA) and small vessel disease correlating with psychosis in AD. CAA are beta amyloid deposits that can constrict a vascular lumen over time. This can weaken the vessel wall or even cause fatal haemorrhages. In addition, the presence of microbleeds can contribute to neurodegeneration and cognitive dysfunction. For those who had ever had psychosis, there was a correlation to the presence of subcortical arteriosclerotic leukoencephalopathy (small vessel disease-related pathology) and other vascular risk factors. Vascular changes present on MRI scans have been associated with late onset schizophrenia as well as early onset psychotic dementia.[32] Given that microvascular abnormalities are implicated in schizophrenia too, there may be a shared vascular dysfunction element in psychosis.

The results of this study showcased a new association between advanced CAA, small vessel disease and psychosis in dementia. Vascular risk factors were associated with psychosis ever present. Since having had a previous episode of psychosis is a risk factor for developing AD+P,[31] it may be that the combination of vascular pathology and reduced information processing speed modulates the risk of developing AD+P. Therefore, cardiovascular disease would be a modifiable risk factor here and is influenced by an interplay of environmental and genetic factors. Other studies hint at increased peripheral inflammatory markers in psychosis spectrum disorders and systemic inflammation causing cognitive impairment.[33] This underscores the possibility of linking vascular pathology and AD+P. Ostensibly, identifying and mitigating vascular disease and its risk factors could potentially reduce the emergence of psychosis in patients with AD.

<u>Neuropathological evidence for a distinct phenotype (AD+P)</u>

New research has attempted to delineate the genetic mechanisms behind AD+P. Studies looking at microtubule associated protein tau (MAPT) pathology found that

there were increased MAPT aggregation in AD+P.[34] Tau is a major protein associated with mature neurons and in AD, tau protein is hyperphosphorylated and aggregates abnormally into bundles.

In a recent study looking at methylomic variation associated with AD+P, 3 key areas of the brain were investigated in post-mortem brain samples – the prefrontal cortex, entorhinal cortex and the superior temporal gyrus.[35] The entorhinal cortex is a hub for navigation and the perception of time, whilst the superior temporal gyrus is the site of the auditory association cortex. Samples from 29 AD donors with psychosis were compared with 18 donors who had AD without psychosis. A gene previously implicated in schizophrenia, *ASM3T* gene, was focused on. Consistent patterns of DNA-methylation across entorhinal, temporal and frontal cortex were noted with the top-ranked loci being enriched for known epigenome wide association and genome wide association for schizophrenia loci. Differentially methylated regions were found in TBX15 and WT1 which were hypomethylated in AD+P relative to AD-P. These genes have previously been reported in relation to AD as WT1 is involved in the formation of neurofibrillary tangles.[36] These results, though perplexing on paper, indicate that the clinical syndrome of AD+P could very well have a distinct genetic basis that is implicated in the aetiology of schizophrenia.

In light of this, there is converging evidence to illustrate that psychotic symptoms across a lifespan have common mechanisms. Recent genomic research has linked polygenic risk to schizophrenia to psychotic symptoms in Huntington's disease and AD.[37] This study is exciting because it indicates that the top-ranked AD+P associated differentially methylated positions are enriched for schizophrenia loci hinting at shared molecular level similarities. Figure1[38] below highlights the possible pathways connecting AD with psychosis. In pathway B – some genetic variants increase the risk for a subtype of AD through possible reduced clearance of beta-amyloid. In A1, though genetic variants do not cause AD+P directly, they increase the deleterious effects of microtubule associated protein tau on

downstream synaptic targets. Some of these variants may also be implicated in the developmental period or neurodegenerative illnesses, pathways A2 and A3.

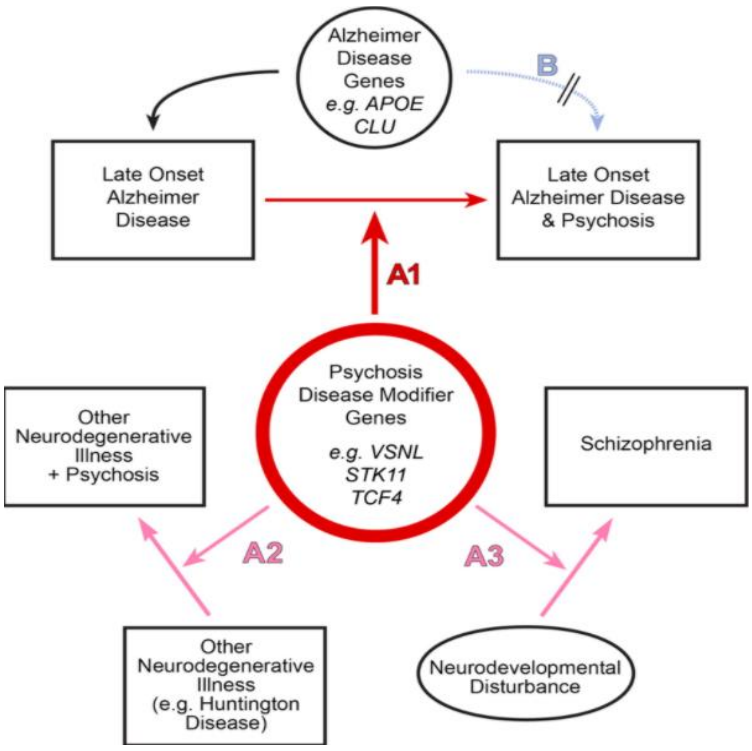

Figure 1: Pathways connecting AD with psychosis, taken from Psychosis in Alzheimer's Disease. Biological Psychiatry. 2014

Heritability of the AD+P phenotype

Vitally, to discern a distinct phenotype, its inheritability must be noted. Familial aggregation has been shown in several studies, with an estimated heritability of psychosis in AD being 61% when defined by the presence of psychotic symptoms.[39] There is emerging evidence that AD+P is more prevalent in the affected siblings of AD+P than among affected siblings of AD without psychosis.[40] Future studies may wish to focus on twins and other relatives of those with AD+P. Another factor to consider is if whether having family history of major psychiatric illness would increase your risk of AD+P. Such studies have been limited by small sample sizes and have been conducted without the use of structured diagnostic interviews of multiple family members. Currently, there is nothing to suggest that family history of major psychiatric illness is not more frequent in AD+P than in AD subjects without psychosis. However, we have data confirming that those with

schizophrenia who develop dementia do so without developing AD pathology, despite the genetic links between the two conditions. [1]

Is genetic risk for psychotic symptoms in AD (AD + P) attributable to common schizophrenia variants?

Genome wide association studies have yielded some mixed results.

A Nature article from 2011 failed to identify any single nuclear polymorphisms (SNPs) that met the strict criteria for significance.[42] But in 2019, another study found that amongst the most significant SNPs in the AD + P analysis showed the most significant SNP in the AD+P versus AD – P analysis was serine/threonine kinase 11 (STK11). As it happens, a genome wide screening on siblings co-affected by schizophrenia found more copies of STK11 more often than in control subjects.[43]

Furthermore, a study from 2018 comparing the genetic risk for schizophrenia and AD+P found no individual genome-wide SNP to reach significance but there were 3 SNPS with strong associations within a single locus.[44] These were noted to regulate the protein coding gene CCNG1 expression which influences Tau kinase activity. In the neocortex of AD subjects, cyclin G1 levels are increased in pyramidal neurons lacking tau aggregates and are not detected in pyramidal neurons containing aggregates phospho-Tau. As aforementioned, excess phosphorylation is linked to AD+P and so it appears that CCNG1 is a possible functional candidate for AD+P risk.

Somewhat counterintuitively, the same study reported an association of polygenic risk for schizophrenia with a reduced risk of developing AD+P. Culprit genetic mechanisms for schizophrenia-associated loci are emerging but how these could reduce AD+P risk is unknown. It may be possible for a set of loci that affect a gene during neurodevelopment to increase schizophrenia risk, but when this expression occurs in a brain with active AD, it is neuroprotective. The role of microglial activation and its dual role of clearing toxic amyloid B and also synaptic elimination may be implicated here. It follows then that particular loci may alter expression of gene transcription differently during neurodevelopment than in the adult brain.

There is also some tentative research showing that the autophagy pathway could be a common pathway to both the pathogenesis of schizophrenia and AD.[45] Of course, these examples are by no means exhaustive suggestions of the different ways specific loci can confer risk for schizophrenia and AD+P.

Limitations of causation arguments in neuropathology and neurogenetics

Forming concrete connections between the two clinical syndromes is challenging for many reasons. The Nature review states that tunnel visioning on psychotic symptoms may actually distract us from other common symptoms that emerge during AD.[4] Is psychosis in AD simply a result of a separate endophenotype? Psychosis within the context of AD needs to be clarified in longitudinal studies with regards to the timing of its emergence. Studies need to consider the frequency of psychotic symptoms and their persistence throughout the course of illness. Defining what stage of illness participants are at is important before being aggregated into the AD+P group as this will clearly influence results.

Studies assessing the overlap between schizophrenia and AD+P usually aggregate different cohorts that have employed different rating scales for psychosis. This can impact downstream classifications of their symptoms and the conclusions drawn from them. Much of the neuroimaging data is limited by small sample sizes and could be made more reliable by their expansion and the acquisition of more frequent MRIs. More research is needed to explore if the phenomenology of psychotic symptoms is truly related to distinct neural correlates. The study looking at CAA and small vessel disease didn't focus on any particular areas for vascular pathology and is also limited by its sample size. Going forward, any neuropathology or neuroimaging studies on this topic should consider co-morbid pathologies and core processes like neuroinflammation and synapse dysfunction.[38] Lastly, neurogenetic work hoping to identify relevant genes must ensure large enough sample sizes whilst maintaining consistent classification criteria of AD+P.

Neurotransmission in AD+P: are there unique alterations in this subgroup?

Demarcating a separate clinical syndrome can be supported by evidence of an idiosyncratic pattern of neurotransmitter alterations in a patient sub-group. Indeed, recent data shows that there are a number of alterations reported in the neurotransmitter group of those with AD+P. A small post-mortem study hinted at the possibility of a selective increase in dopamine D3 receptor availability, these

findings were independent of neuroleptic use or Lewy body pathology.[46]AD+P has been linked with reduced serotonin (5-HT) in the ventral temporal cortex and this could be linked to lower cell counts in the dorsal raphe.[47] Altered 5-HT_6 receptor function has also been documented.[48] Variations in expression of certain serotonin receptors is vital to note as it enables the creation of innovative pharmacotherapy. Pimavanserin, a selective serotonin 5-HT_{2A} inverse agonist, is an upcoming agent targeting hallucinations and delusions in the dementia population.

Additionally, cholinergic alterations have been explored in literature; AD+P is linked with an increased ratio of acetylcholinesterase/serotonin.[38] We know already that cholinergic neurons that constitute the basalis of Meynert are severely depleted in AD. There is also research to indicate that higher muscarinic M2 receptor density has been noted in the orbitofrontal gyrus and middle temporal gyrus of AD+P patients.[49]Lastly, another report highlighted increased norepinephrine in the substantia nigra of AD+P studies.[50] Both animal and human studies convey a link between the role of noradrenergic dysfunction and aggressive behaviour, but more scrutiny is needed to further establish the link to AD+P.

When reviewing the evidence of implicated neurotransmitters, it is prudent to recall that whilst some neurotransmitters like glutamate or oxytocin for example, may not play a direct role in the development of AD+P, they may do so via contributing to oxidative stress.[51] Further research could focus on whether there is a relationship between neurotransmitter alterations and synaptic damage or mitochondrial function that verifiably modifies the pathogenesis of AD+P.

Considerations for future research on AD+P

My exploration here, albeit brief, has shed light upon a few critical themes regarding AD+P. There is an argument for a clear differentiation of psychosis within AD as a severe subtype of AD. Our understanding of this is supported through neuroimaging studies which have shown the significance of altered metabolism, atrophy and vascular lesions in both neocortical and cortical structures of the brain. In particular, prefrontal cortex structures appear to be impacted the most commonly in AD+P.[52] More work is needed on the diagnostic and classification structures for AD+P. It is not yet clear if a specific neuropsychological profile is associated with the different types of psychosis (paranoid or misidentification).

When considering the rates of increased aggression in AD+P, there is a real urgency to treat these patients effectively. Not only is aggressive behaviour strenuous for family caregivers but it also increases the risk of hospitalisation.[53] The current pharmacotherapy for psychosis and behavioural and psychological symptoms of dementia centres around the superiority of atypical agents, like aripiprazole, quetiapine, olanzapine and risperidone. These come with a whole host of side-effects and can worsen patient mortality.[54] Whilst the data on atypical antipsychotics suggests clinical utility for these drugs, the magnitudes of treatment effects are not consistent. A possible resolution to this issue would be targeting the emerging neurobiology of AD+P.

However, whilst we know that pathological accumulation of MAPT is implicated in psychosis, whether this is a causal link has not been determined. The heritability of AD+P and its association with loci relevant in schizophrenia strengthen the likelihood of shared neurobiology of the two conditions. In order to further elucidate these findings, innovations in the field of genetics and neuroimaging must work in synchrony. This may well be able to generate new therapeutic targets that focus on tau pathology, alpha-synuclein pathology or both.

Conclusion: how can we enhance clinical care for AD+P patients through a biopsychosocial approach?

Locating a specific and effective treatment for AD+P would be ideal. Until then, the psychiatric world must prepare for the upsurge of dementia in the global population and carefully consider how to best support patients and families reckoning with the persistent emotional burden of psychosis in the elderly. Enhanced recognition of psychosis in AD could be used as an indication for imminent worsening in cognitive function. This knowledge can be used to better prepare clinicians and caregivers. From what we understand about the miasma of delusions experienced by AD+P patients, such cases necessitate creative ways of providing psychosocial support.

Glancing back to the case study I opened with, it is likely that this patient has some form of treatment- resistant psychosis. In the face of such psychological complexity, we as clinicians must re-evaluate our role within the wider framework of a biopsychosocial model of health. Elderly patients in the community and in hospitals require social and intellectual stimulation as much as they need prescriptions for behavioural management. This is even more evident for those

with difficult-to-treat AD+P. Going forward, our society should encourage additional community-based efforts to grapple with this growing demand. In addition, care homes and nursing homes must be equipped to manage the complex psychological sequelae of AD+P. This may be achieved by adapting current occupational therapist and psychologist job roles, or devising new ones that are tailored for elderly patients. Looking beyond effective medication strategies, volunteering programs that focus on individualised support and pastoral care should be pushed to ensure that elderly patients are not left to confront their psychosis alone.

References available on request.

Essay 3

Post Stroke Depression: A result of Neurological Damage or a reaction to psychosocial upheaval?

by

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1. Introduction

Depression occurs in approximately 30% of stroke survivors[1]. Though approximately 85% of strokes are ischaemic, it is at least as common after haemorrhagic stroke[2]. The origin of Post-Stroke Depression (PSD) has been subject to extensive research and debate. Two hypotheses predominate. One proposes that stroke-related neurobiological changes drive its development. The other considers it a predictable reaction to a disastrous life event[3]. That is, PSD might be either an "endogenous" or a "reactive" subtype of depression[4]. I will examine the evidence for each. In Section 2, I will show that PSD is indeed closely tied with neurobiological changes associated with stroke as well as Major Depressive Disorder (MDD). In Section 3, I will depict how the event of stroke can transform an individual's physical, economic and psychosocial environment in a manner that is conducive to depression as well as how environmental and biological factors interact. In Section 4, I will introduce the concept of semantic shaping[5], describing further influences on the formation of signs and symptoms that ultimately define PSD. In the reviewed literature, PSD was most often defined by depression scale scores above a validated threshold or a diagnosis of either MDD or Minor Depressive Disorder on clinical evaluation within a post-stroke time frame of interest. In this essay, the term PSD simply denotes the occurrence of depressive symptomatology post-stroke. I will conclude with emphasis on the inseparable contributions of biology, the environment and semantics.

2. Biology:

2.1 Stroke and Post-Stroke Depression: Biological overlap

Acute stroke results from abrupt disruption of cerebral blood flow, which triggers a cascade of events that lead to cell death[6]. In the case of arterial occlusion, there is immediate hypoperfusion of the supplied tissue, rapid oxygen depletion, Na+/K+-ATPase failure, loss of transmembrane ion gradients and excess of glutamate that cannot be actively cleared from the synaptic cleft. In a process known as glutamate-mediated excitotoxicity, glutamate causes inordinate depolarisation which in turn both exacerbates glutamate excess via augmentation of N-methyl-D-aspartate (NMDA) receptors and results in release of intracellular calcium stores, calcium-mediated subcellular destructive processes and oxidative stress. In addition, neuroinflammatory and systemic stress responses are activated[7]. Similarly to ischaemic stroke, haemorrhage results in cerebral hypoperfusion, glutamate-mediated excitotoxicity, an inflammatory reaction[8] and stress response[9]. In this case, hypoperfusion results as rising intracranial pressure lowers cerebral perfusion pressure and glutamate excess is triggered by influx of glutamate from the bloodstream as well as thrombin-mediated SrC kinase activation[8]. The ultimate consequence of stroke is localised parenchymal damage. Alongside destructive processes, signalling pathways supporting neuroplasticity are upregulated[10]. Key pathophysiological events common to both types of stroke are linked to development of PSD.

An important aetiology of both ischaemic and haemorrhagic stroke is cerebral small vessel disease (SVD)[11], which is itself associated with depression. SVD describes a pathological process affecting small cerebral blood vessels, including arterioles, capillaries and venules[12]. As well as predisposing to small subcortical infarcts (lacunar stroke) and deep intracerebral haemorrhage[11], SVD manifests as leukoaraios[1] and cerebral microbleeds[13] associated with *chronic* hypoperfusion and ischaemia[14] and a more gradual onset of subtler clinical symptoms[15]. White matter (WM) tracts supplied by terminal arterioles are especially vulnerable to ischaemia and contain connections integral to the function of multi-region neural networks[12]. Observations that late-life depression is commonly comorbid with SVD, frequently proceeds overt cerebral ischaemia and is less responsive to treatment led to the concept of a Vascular Depression (VD). Alexopoulos and colleagues[16,17] postulated that VD is precipitated and/or exacerbated by SVD-mediated disruption of neural

[1] White matter of abnormal appearance

circuitry regulating mood. Strong evidence has since emerged in support of this entity. Meta-analysis of 38 cross-sectional studies investigating the relationship between SVD and depression and correcting for cardiovascular disease (CVD) risk factors found that both magnetic resonance imaging evidence of leukoaraios (WM hyperintensities [WMH]) (OR 1.29) and cerebral microbleeds (OR 1.18) are associated with depression. Further meta-analysis of eight longitudinal studies found an association between WMH and incidence of depression over a mean follow-up period of 3.7 years (OR 1.18)[18]. Blood markers of endothelial dysfunction have also been associated with a greater level of depressive symptoms in the elderly[19]. Such tangible evidence of biological aetiology underlies descriptions of VD as an "organic"[20] or "neuropsychiatric"[21] form of depression.

PSD is conceivably closely related to VD, perhaps distinguished only by its temporal relationship with an abrupt, easily recognised event[22]. Indeed, WMH have also been associated with PSD[23]. PSD has been observed to follow transient ischaemic attacks and minor strokes[24,25], which could be considered to fall between SVD and major stroke on a spectrum of ischaemic insults. Further, the risk of PSD appears to increase with both successive ischaemic events[26] and radiological extent of SVD[27,28]. This supports Alexopoulos'[16] initial suggestion that VD may result from cumulative vascular insult inclusive of both discrete events and chronic disease.

Concededly, a causal relationship is difficult to establish. There is ample evidence that depression predisposes to CVD[29] and even a unidirectional relationship could be mediated by functional impairment. However, by enlisting a large sample (n=626) with no disability at baseline the Leukoaraiosis And DISability (LADIS) longitudinal study indicated that SVD is associated with depression in its absence. Baseline WMH rating[2] predicted Geriatric Depression Scale (GDS) score, accounting for cognitive impairment[3] and quality of life[430]. Baseline WMH rating also predicted GDS score at one[31] and two year[32] follow-ups, accounting for baseline depressive symptoms as well as disability that developed. At three years, progression of WMH predicted incident depression in the preceding year[33]. Thus

[2] Derived using Age Related White Matter Change Scale
[3] According to Mini Mental State Examination
[4] According to self-reported Euro-Qol VAS, a scale indicating subjective health

the LADIS study provides evidence that vascular insult can precede - and may drive - the associated depression.

A significant number of LADIS study subjects had a history of stroke[5], illustrating that it is difficult to separate PSD from VD. Moreover, at baseline a history of stroke was less strongly correlated with GDS score (ρ=0.07) than WMH (ρ=0.16) and unlike WMH, it was not a significant predictor of GDS score in logistic regression analyses[30]. Furthermore, while subjects who had a stroke during the follow-up period had a significantly higher GDS score at three years compared with those who didn't, incidence of depression was not significantly different between these groups[33]. Hence it does seem that cumulative vascular insult is of greater relevance to depressive symptoms. What is referred to as PSD may in fact be VD that becomes apparent after acute stroke.

Multiple elements of the pathophysiological cascades ensuing disruption of blood flow in the event of stroke are also linked to PSD. Elevations in blood markers of oxidative stress including malondialdehyde and 8-OHdG[34] and of inflammation including C-Reactive Protein[35,36], homocysteine[36,37], Interleukin 6[38,39] and Tumour Necrosis Factor alpha[38] at the time of hospital admission have been associated with increased risk of PSD. Significantly higher glutamate levels in the frontal lobe on single-voxel proton magnetic resonance spectroscopy have been found in depressed relative to non-depressed stroke patients[40]. Lower serum Brain-Derived Neurotrophic Factor (BDNF) levels following stroke have been associated with increased risk of PSD[41], suggesting an inadequate neurotrophic response might also contribute to its development. Efficacy of pharmacological treatments for PSD might be partly attributed to influence on neurotrophic activity[42]. One meta-analysis of 29 trials suggested that selective serotonin reuptake inhibitors promote neurological recovery post-stroke[43], though a recent Cochrane review did not support this[44].

The systemic response to the physiological stress imposed by stroke is implicated in PSD. The hypothalamus-pituitary-adrenal (HPA) axis has a central role in the response to stress, the release of corticotropin-releasing hormone from the

[5] 183 subjects had a history of stroke at baseline; a further 46 subjects had a stroke during the follow-up period

paraventricular nucleus of the hypothalamus activating both the autonomic nervous system (ANS)[45] and a cascade of hormones that in turn trigger a range of physiological changes to help contend with the stressor[46]. The HPA axis may become acutely dysregulated after stroke, one proposed mechanism being damage to brain regions that provide it negative feedback[47]. As a consequence of its coupling to inflammatory, metabolic and neurophysiological processes, HPA activity potentially contributes to many of the pathophysiological mechanisms involved in stroke including the immunologic response, glutamatergic signalling and oxidative stress[48]. A meta-analysis of nine studies showed that elevated cortisol level post-dexamethasone suppression[6] within a mean of 59 days of stroke is associated with development of PSD (OR 2.66)[49]. Given that post-stroke hypercortisolaemia has also been associated with dependency and mortality after adjusting for stroke severity[50], its relationship with PSD might be partially mediated by effects on stroke pathophysiology.

The pathophysiological processes associated with stroke culminate in parenchymal damage. The hypothesis that damage to brain regions involved in regulation of mood might ultimately cause PSD has been repeatedly tested. However, meta-analyses have failed to show that lesion location predicts PSD[51,52]. More contemporary voxel symptom mapping studies have substantiated this finding[53-55] and instead suggested that lesions that map to a relevant neural circuit are associated with PSD. Using five independent datasets (n=461) in conjunction with resting state functional connectivity data from 1000 healthy subjects, Padmanabhan and colleagues[55] showed that lesions of depressed stroke subjects fell within a neural circuit centred on the left dorsolateral prefrontal cortex (DLPFC) regardless of stroke aetiology. While the degree to which lesions intersected this circuit predicted depression (OR=1.62) and depression severity (r=0.13), lesion size did not. Further, transcranial magnetic simulation sites shown to provide PSD symptom improvement also fell within the circuit centred on the DLPFC, increased regional activity within which the authors acknowledged has been implicated in pharmacologic antidepressant response[56]. Their work highlights that a lesion need not be spatially close to a critical brain region to functionally impact it, nor might an effective treatment need to act directly on it. It is conceivable that all

[6] Indicative of HPA axis hyperactivity

pathological mechanisms discussed here and perhaps all effective treatments for PSD ultimately converge on their influence on relevant neural *connections*, even if their individual effects are more widespread.

2.2 Post-Stroke Depression and Major Depressive Disorder: Biological overlap

While the pathophysiology of MDD remains under investigation, influential hypotheses can also be connected to PSD. The monoamine hypothesis focuses on reduced monoaminergic neurotransmission in MDD[57]. PSD has been associated with lower cerebrospinal fluid concentrations of the serotonin metabolite hydroxyindolacetic acid[58] as well as polymorphism of the serotonin transporter gene[59]. The inflammatory hypothesis posits that MDD is driven by a chronic inflammatory process[60]. In addition to aforementioned post-stroke inflammatory-marker elevations[35-39], polymorphisms associated with reduced anti-inflammatory cytokine function appear to increase PSD risk[61]. The chronic stress model of depression is a validated experimental tool. Subjecting rodents to chronic mild stress reliably triggers depressive behaviours[62] and stressful life events are an established risk factor for MDD in humans[57]. MDD[42] as well as PSD[49] are associated with dysregulation of the HPA axis.

Other factors implicated in MDD that have also been associated with PSD include genetic predisposition, altered glutamatergic neurotransmission and neurotrophic changes. Both MDD[63] and PSD[59] appear to be partially heritable. Several glutamate receptor modulators under increasing investigation including ketamine have rapid antidepressant effects[64]. Inadequate neurotrophic activity is associated with MDD[42] as well as PSD[41] and it has been shown that a range of antidepressants in common use facilitate neurogenesis[42].

Strikingly, some mechanisms are implicated in all three of stroke, PSD and MDD. Also of note, there is substantial overlap between mechanisms. For example, both HPA activity and inflammatory mediators modulate neuroplasticity and decrease the production of serotonin[65]. A common stance is that multiple mechanisms are likely to contribute to MDD and may affect individuals differentially[42,57]. In this context, vascular insult could be viewed as yet another component of a complex interlinked web of biological factors that promote depressive symptomatology. Stroke might merely abruptly aggravate a vulnerable biological milieu.

3. Environment

3.1 Stroke-related Environmental Risk Factors for Post-Stroke Depression

Stroke is an unsettling, if not transformative and traumatic event. Among a large UK population of stroke survivors (n=748), 34% were newly disabled at one month follow-up[66]. Sudden physical and/or cognitive deficits may impact both physical and psychosocial environments profoundly, having immediate implications for an individual's home setting, daily routine, relationships and capacity to work. Among the same UK stroke survivors, risk of institutionalisation within five years was 19%[66]. Others experience prolonged inpatient rehabilitation, medical complications requiring further admissions to hospital[67] and home modifications to facilitate activities of daily living[68]. Post-stroke care is complex and a majority of survivors report unmet care needs[69]. Many will not return to work[70]. Social networks contract, friendships in particular are vulnerable to loss[71,72] and even persisting relationships transform[71,73]. Qualitative studies report expressions of shock, grief[73,74], shame[73-75], confused identity[73] and uncertainty about the future[68,73]. Being a potentially life-threatening event, the diagnosis of stroke can evoke a fear response with both physiological and psychological elements. Both major and minor stroke can trigger post-traumatic stress disorder[76]. Given an established link between stressful life events and MDD[57], it is easily conceivable that the highly disruptive experience of stroke could provoke depressive symptoms.

Environmental factors are indeed heavily implicated in development of PSD. The disability that mediates many environmental changes post-stroke is a consistent predictor of PSD[1,77-80]. Concededly, it is possible that this well-established relationship reflects a greater burden of the neurobiological changes described in Section 2.1, corresponding to more severe stroke in more disabled subjects. However, several studies that have evaluated both stroke severity and disability suggest that functional incapacity imparted by neurological damage is more relevant than neurological damage itself. In multivariate regression analyses,

persisting disability[7] but not initial neurological impairment[8] predicted onset of PSD at 1+ month[81], 3-4 months[82] and 3 years[83]. A meta-analysis incorporating studies that measured only one of these showed that level of disability is associated with higher risk of PSD (pooled OR 1.52 using four studies) than stroke severity (pooled OR 1.12 using six studies)[79]. This is not surprising when it is considered that disability could both necessitate drastic adjustments to physical environment and limit activities that previously shaped an individual's economic and psychosocial environment. Even with strong support a new disability could redefine daily life.

Indeed further evidence suggests that it is the environmental implications of persisting disability that are of highest relevance. In a large UK study (n=3,689)[84], inability to work was associated with a higher risk of PSD than either disability itself[9] or specific deficits including dysphagia, incontinence and impaired cognition. This was true at three months, one year, three years and five years of follow-up. A large study (n=639) recruiting subjects across 30 Chinese townships[85] found that activity (standardised regression coefficient 0.413) and social participation (standardised regression coefficient 0.530) have a greater influence on PSD risk than persisting neurological impairment[10] (standardised regression coefficient -0.284). In this study, physical environment, support services and local policies were also associated with PSD. In other studies, specific activities including listening to music, in person conversation[86] and exercise[83] were associated with lower depression scale scores. Hence environmental support could buffer the impact of new impairments, supporting a "reactive" aetiology of PSD.

A further body of evidence does suggest that an individual's psychological *reaction* to environmental circumstances is more influential than the circumstances themselves. In multiple regression analyses, Crowley and colleagues[87] found a state of acceptance[11] at three months post-stroke to moderately negatively correlate with depressive symptoms at both three months (r=-0.396) and nine

[7] According to Modified Rankin Scale[81,83], Barthel Index[82]
[8] According to NIHSS[81]; Scandinavian Stroke Scale[82]; 9-item stroke severity index[83]
[9] According to Barthel Index
[10] According to Canadian Neurological Scale measured 3+ months post-stroke
[11] According to 6-item acceptance scale within The Illness Cognition Questionnaire

months post-stroke (r=-0.512), controlling for disability[12] and social and emotional support[13]. Townend and colleagues[88] found a significant association between non-acceptance of disability[14] and PSD at one month (OR=1.27) and nine months (OR=1.46) post-stroke, controlling for stroke severity[15] and disability[16]. While the relationship between PSD and attitude is conceivably bidirectional, using continuous time structural equation modelling, Volz and colleagues[89] determined that self-efficacy[17] predicts PSD (α_{12} = -0.29) to a greater extent than vice versa (α_{12} = -0.17). Finally, if an individual's psychological reaction post-stroke drives PSD then pre-morbid personality traits that influence it should also be associated with PSD. Indeed, neuroticism has repeatedly been associated with increased risk of PSD[79]. Hence the psychological challenges imposed by new disability and environmental changes could be either buffered or exacerbated by an individual's premorbid psyche.

3.2 Interplay Between Environment and Biology

The concepts of "endogenous" and "reactive" depression blur when interactions between neurobiology and environmental factors are considered[90]. Neurobiological insult may be inconsequential without simultaneous environmental insult. Environmental stress manifests biologically. Similarly, antidepressant therapies need not be physical or pharmacologic to exert a neurobiological effect. Further, pre-morbid interplay between biological and environmental factors could ultimately shape an individual's reaction to stroke.

The environmental context in which biological alterations occur appears to dictate their clinical effect. Animal studies have shown that preventing neurogenesis by irradiation or transgenic modification results in depressive behaviours only in the setting of concomitant environmental stress[91]. Caspi and colleagues[92] seminally[93] showed that in humans a polymorphism of the promoter region of the serotonin

[12] According to Barthel Index
[13] According to Significant Others Scale (SOS)
[14] According to Non-acceptance of Disability questionnaire, substituting "illness" with "the effects of my stroke"
[15] According to NIHSS score
[16] According to Barthel Index and Nottingham Extended Activities of Daily Living Scale – both reverse scored so that a score of 0 represents independence
[17] According to a validated General-Self-Efficacy Scale

transporter gene conferring lower transcription efficiency increases risk of depression only in the setting of either childhood maltreatment or stressful events related to employment, finances, housing, health or relationships. This interaction was corroborated by a meta-analysis of 54 subsequent studies[94]. It is not surprising then that a meta-analysis of four studies showed that the same polymorphism increases risk of PSD (pooled OR 2.05)[59]. Similar interactions have been found between life stress and polymorphisms of the BDNF gene[95], the corticotropin-releasing hormone receptor gene[96] and the FK506 binding protein 51 (FKBP5) gene[97] in depressed subjects. Accordingly, a genome-wide association study of 73,258 subjects with MDD revealed that its heritability is greater in the setting of traumatic life events, even after accounting for genetic influences on trauma exposure[63]. Such findings suggest that certain biological alterations associated with depression merely impair an individual's ability to adapt to environmental stress and are therefore irrelevant until there is stress requiring adaptation. Whether a certain threshold of stress is required to induce categorical depression or whether burden of stress correlates with burden of depressive symptoms is subject to debate[93].

In many ways, the environment is *imprinted* in the structure and function of the brain, which is constantly assimilating sensory information, performing cognitive processing of events and responding to them. Adaptation of neural circuitry according to experience is integral to development[98], learning and memory[99]. Stressful experiences by definition are an adaptive biological response to aversive stimuli[100], engaging the HPA axis and connected processes with heavy involvement of the central nervous system. Many of these processes are mediated by corticosteroid nuclear receptor-coupled regulation of gene transcription[101], such as downregulation of neurotrophins in the glucocorticoid receptor-rich hippocampus and prefrontal cortex[102,103]. Prolonged or repeated stress can in turn lead to *macroscale* structural and functional transformations detectable on brain imaging. These include atrophy of the hippocampus and prefrontal cortex and hyperactivity of the amygdala[102], all additionally associated with MDD[104,105]. The environment is also expressed in patterns of gene expression via epigenetic changes that do not necessarily involve corticosteroid actions[106], including DNA methylation, histone modification and chromatin structural changes[107]. Of note, many epigenetic changes associated with MDD impact the HPA axis and connected processes including immunity and neuroplasticity[106]. Hence an individual's

capacity to adapt to stress is influenced not only by aforementioned inherited polymorphisms but also epigenetic modifications driven by the environment. The widely entertained[62] idea that depression might ultimately represent a maladaptive response to stress is one that inherently encompasses interplay of biological and environmental contributors. In any case, genetics, neurobiology and the environment are clearly integrated.

It may in fact be difficult to separate parenchymal damage secondary to ischaemic insult from that secondary to ensuing environmental stress. Venna and colleagues[108] showed that social isolation of mice immediately post-stroke not only results in depressive behaviour but also increases histological infarct size 72 hours post-stroke. As described in Section 2.1, the pathophysiology of stroke incorporates a stress response to the internal physiological stress imposed by stroke. External stressors conceivably *augment* it. In addition, optimal neuronal recovery from stroke relies on neurotrophic activity, which could be suppressed by environmental stress[102] or enhanced by environmental enrichment[109]. Indeed in a separate population of mice with equivalent infarct volumes, functional recovery was greater in those that were pair-housed and it paralleled BDNF expression and cell proliferation[108]. While it is more difficult to confirm cellular activity in human patients, this may explain how an enriched neurorehabilitation environment[18] resulted in greater functional[19] and cognitive[20] improvement than a rehabilitation program alone in a randomised controlled trial[110]. The question of whether PSD arises secondary to neural damage or environmental changes associated with stroke becomes almost senseless when it is considered that environmental factors may contribute to neural damage.

The power of environmental interaction is also demonstrated by the biological effects of psychosocial interventions for depressive disorders. Psychotherapy constitutes an interaction within a supportive psychosocial environment that engages cognition and emotion-related neural circuitry. Functional imaging studies have demonstrated that it results in regional changes in activity similar to

[18] Access to a physical and cognitive activity "arcade" for 2hr daily in addition to a rehabilitation program
[19] According to Functional Independence Measure motor score
[20] According to Montreal Cognitive Assessment score

those effected by pharmacologic therapy, decreased prefrontal cortical activity being a common finding among them[111]. A meta-analysis of 56 randomised controlled trials found psychological therapies[21] to be associated with strengthening of immune function[22112], supporting the inflammatory hypothesis of depression. If one takes the view that signs and symptoms are ultimately the result of neural function, then successful treatment of depression can be achieved with either "bottom-up" (physical including pharmacologic therapies) or "top-down" approaches (psychosocial interventions)[111]. It follows that the cause may also take either path.

Interplay between neurobiology and the environment does not begin post-stroke. The event of stroke occurs in the context of decades of premorbid interactions and a corresponding resilience or vulnerability to stress. The HPA axis and ANS are extensively linked with cortical and subcortical neural circuitry subtending attention, sensory perception, cognition, memory and emotion, allowing *perception* of environmental stressors as aversive and ultimately influencing the likelihood, degree and subjective feeling of a stress response. Both genetic factors and patterns of previous stress exposure moderate information processing[113]. A large (n=7500) longitudinal twin study suggested that resilience[23] is partially heritable[114]. Epigenetic changes may also promote it[115]. The timing, severity and type of past stressors are all influential. Chronic stress appears to sensitise the HPA axis and ANS whereas repeated exposure to a mild stressor appears to result in a progressively diminished response with successive exposures[113]. Personal control over an intermittent stressor appears to enhance resilience in association with prefrontal cortex-mediated regulation of arousal[115]. These observations apply even when subsequent stressors are novel.

Experiences in early childhood and adolescence – critical periods for neuroplasticity - seem particularly relevant[115]. Childhood maltreatment has been

[21] Behaviour therapy, cognitive therapy, cognitive behavioural therapy ± additive treatment, bereavement or supportive therapy, multiple or combined interventions, other psychotherapy and psychoeducation
[22] Proinflammatory cytokines and markers, anti-inflammatory cytokines, antibodies, immune cell counts, natural killer cell activity, viral load and other immune outcomes including number of infectious diseases
[23] Modelled as the difference between actual and predicted (based on life stressors) internalising symptom score

associated with morphological and functional alterations that may compromise threat detection[116] as well as cause emotion dysregulation and vulnerability to stress-related disease, while strong parental bonds may buffer the effect of early trauma[115]. Interestingly, Moog and colleagues[117] showed that new-borns of mothers exposed to childhood maltreatment[24] have significantly smaller overall brain size and grey matter volume than new-born controls, accounting for peri-natal complications, violence during pregnancy, socioeconomic status and maternal age and health. While the functional effect of these changes has not yet been studied, it suggests that characteristics of an individual's brain are shaped by events that occur even *before conception*. In this light, PSD cannot feasibly be seen as a simple function of the severity or location of neural impact *or* the intensity of environmental changes associated with stroke because the same circumstances could theoretically affect two individuals very differently.

4. Semantics

4.1 The Concept of Semantic Shaping: The Plot Thickens

The research described here used symptom scale scores or clinical assessment to define depression post-stroke, based on current descriptive psychiatric nosology. Both symptom scales and clinical assessment are subject to what the Cambridge School of Psychopathology[5,118,119] refer to as "semantic shaping"[5]. This concept acknowledges that whether or not psychopathologic phenomena have an "endogenous" or "reactive" explanation, the *realisation*, *interpretation* and *communication* of them by both patient and clinician are themselves under complex influences.

Based on elaborations by Berrios[118,119], Markova[5,118] and Aragona[5,120] the idea could be summarised as follows. Either a biological or environmental catalyst first leads to a "change in mental state"[5]. When the individual subsequently becomes conscious of the change, the way it is understood and expressed will inevitably be coloured by factors such as intelligence, education, eloquence, personality, pervading societal culture, previous exposures and the interactions between these. At times the change in mental state might bypass consciousness but

[24] Emotional, physical or sexual abuse or neglect

manifest in behaviour interpretable by others. Alternatively, it may be assisted through consciousness by a clinical interaction and thereby contorted by the idiosyncratic perspective, set of experiences and choice of enquiries that the clinician offers. Both patient and clinician may borrow from available stereotypes or "templates"[119] that don't truly approximate the phenomena but nonetheless aid thought and communication. Thus a psychopathologic sign or symptom could be seen as having a "neurobiological kernel" and a "semantic shell"[118]. Taking this view, we cannot expect signs and symptoms to purely reflect their origin. In the course of becoming apparent their identity evolves and *incorporates* semantics.

The concept could be considered especially relevant to PSD. New neurological deficits could add an additional layer of complexity to interpretation and expression of mental phenomena, anosognosia and aphasia being extreme and readily imaginable examples. In addition, Many stroke patients are never screened for PSD[65] and neurologists and their colleagues providing post-stroke care might not be as astute to nuanced differences in behaviour and mood as they are to sensorimotor deficits and cognition[21]. It has been noted that PSD presents with more cognitive complaints and less anhedonia than MDD[65] and that symptom profile changes with time of onset post-stroke[22]. This might reflect a different aetiology and/or pathogenesis. Alternatively, at least to a degree it might reflect stroke's distinctive contributions to semantic shaping, which may change with time.

4.2 Interplay Between Semantics, Biology and Environment

As delineated in Section 3.2, biology and the environment are not independent of one another. Nor is either one independent of semantics. If we define an illness by signs and symptoms according to current descriptive psychiatric nosology, then the illness is driven as much by their semantic constituents as it is by a biological or environmental aetiological underpinning. Since both biological and environmental factors and their interplay could shape interpretation and expression of mental phenomena, all three of biology, the environment and semantics are interwoven. They do not just each "contribute" to illness, they also *interact*.

Their interactions are difficult to decipher because each is usually studied in isolation, the others treated as potential experimental confounders. This approach has been useful for elucidating a multitude of biological and environmental factors

relevant to PSD, described here. However it limits our understanding of the convoluted connections between them, the highly contextual discernment of signs and symptoms that define the illness and the purity with which they reflect their origins. Treating semantic shaping as "noise" to a more important underlying biologically and/or environmentally-driven neural abnormality is dismissive of the real-life experience and meaning of mental phenomena for patients[5,120]. It is the latter that psychiatry ultimately tends to. Moreover, a better understanding of the process of formation of a sign or symptom might help us to distinguish modulators from triggers.

5. Conclusion

Stroke can engender dramatic neurobiological and environmental changes conducive to depressive symptomatology and also change the way an individual interprets and expresses mental phenomena. Risk of PSD has been linked to many of the individual pathophysiological processes that contribute to stroke-induced parenchymal damage, perhaps because injury to neural circuitry regulating mood is a collective consequence. Myriad environmental factors also influence risk of PSD, many of them disability-mediated and ultimately imposing significant psychological challenges. The way an individual reacts to these is influenced by a complex interplay of biological and environmental factors beginning decades before the stroke event and reflected in the structure and function of the brain. The signs and symptoms that emerge and are recognised as PSD are subject to processing and evolution during self-interpretation as well as clinical interactions, which also have a post-stroke context. In light of the evidence explored here, the question of whether PSD has an "endogenous" or "reactive" aetiology could be considered inane. Both are a gross oversimplification. More pertinent is the relative contributions of neurobiological changes, environmental factors and semantics, which is likely to differ between individuals and change over time. Importantly, the three are in practice inextricable. Therefore, it would be constructive for both clinicians and researchers to remain cognisant of their interactions. Understanding the complex formation of signs and symptoms that define depression may prevent the biologically and environmentally-influenced, neurally-mediated change in mental state that underlies them from becoming "lost in translation".

References available on request.

The Court of Protection: Covid-19 vaccines and the older person (Part 2)

by

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Introduction

This article describes how the Mental Capacity Act 2005 was applied in two cases regarding the assessment of capacity and best interests (s4) of older people receiving the Covid-19 vaccine.

SD v Royal Borough of Kensington And Chelsea **[2021][1]**

Background

V is a lady in her seventies with dementia due to alcohol-related brain damage ('Korsakoff's syndrome') who had lived 'quietly and comfortably' in a care home since 2011. V's personality was described by her daughter SD as being deferential to those in authority and had a '…diffident compliance of medical professionals'.

SD, who lived in the USA, objected to V being given the vaccine because she felt it had not undergone sufficient safety trails (she provided the court with a plethora of information primarily from internet sources). SD forbade the care home to administer the vaccine (every other resident and all staff had been vaccinated). SD contended her mother would not have wished to have received the vaccine had she capacity to make this decision and hence it was not in her best interests (she described V's compliance with influenza vaccinations over the previous nine years as being evidence of her 'general disorientation in the world' and not her true beliefs or wishes).

Capacity to be vaccinated

There was no dispute, that due to dementia, V did not have capacity to decide whether to be vaccinated or not.

Best interest determination

The court considered V's beliefs and values along with views from SD, a carer, her social worker and her GP. The carer expressed concern about V's vulnerabilities as social distancing in the care home was 'near to impossible' as she wandered a lot which negated social distancing measures, and had a lack of understanding of the risk posed by Covid-19. The judgment noted V's particular vulnerabilities to severe disease or death from Covid-19: her age, excess weight and dementia and she lived in a care home (at that time 25% of all Covid-19 deaths were in care homes).

The court noted that while SD's application was predicated on her wish to see greater data in relation to efficacy and safety of the vaccine, her proposed alternatives had not as at yet achieved clinical credibility (she was 'to put it mildly, extremely enthusiastic about the viability and potential for an anti-parasitic drug'). The court was bemused SD rejected the overwhelming view of public health authorities in relation to a certified vaccine to wholeheartedly embrace the unquantifiable risk of an unlicensed medication. The judgment noted that SD's opposition to the vaccine was borne out of genuine concern for V but it did not reflect V's authentic view and was simply a reflection of how 'filial love and concern' can sometimes obstruct objective decision making.

Conclusion

The court found that due to V's particular vulnerabilities and her circumstances she lived in, the risk to V's life and health would be 'unacceptably high' if she did not receive the vaccine. Hence, it was in her best interests to receive it. The judgment applied the 'risk matrix' from *Re E*[2] when weighing up the risk from Covid-19 as it was 'equally' pertinent to this case. The judgment emphasised the importance of 'respect for and promotion of P's autonomy and an objective evaluation of P's best interests will most effectively inform the ultimate decision. It is P's voice that requires to be heard and which should never be conflated or confused with the voices of others, including family members however

unimpeachable their motivations or however eloquently their own objections are advanced.'

***SS v London Borough of Richmond Upon Thames & Anor* [2021][3]**

Background

SS is an 86-year-old lady with dementia residing in a large care home. At the end of the first lockdown, 27 out of 99 residents had died from Covid-19. There were various capacity issues being assessed but it was in the context of this Covid-19 backdrop that she refused the vaccine. The care staff showed 'insightful, caring and sensitive' understanding of SS. Having experienced the catastrophic effects in the home, they were under 'no misapprehension about how dangerous and insidious the virus' was.

Capacity to be vaccinated

The GP had visited to assess residents and administer the vaccine. She and care home staff had encouraged SS to have the vaccine on many occasions. The GP concluded SS 'failed' the capacity assessment as she was unable to understand or retain relevant information due to her dementia process. While agreeing with this conclusion, the court clarified that a capacity assessment was 'not a test that an individual passes or fails, it is an evaluation of whether the presumption of capacity has been rebutted and if so, for what reason.'

Best interest determination

The court considered SS's beliefs around her healthcare. Her records, going back to 1997, revealed a consistent pattern (predating her dementia diagnosis) of SS having routinely engaged with medical professionals up until 2015 when the effects of her dementia process emerged. The records indicated SS had never received any form of vaccine, and the records included an 'unambiguous note' that she declined both seasonal influenza and pneumococcal vaccines when offered.

The GP predicted vaccine administration to SS would be 'challenging' in anticipating her resistance. She believed physical restraint would be 'necessary and proportionate with the minimum amount of force for the shortest period of time'. This would need to be a joint decision between the vaccine administrator and care home staff.

A consultant psychiatrist explained the options in non-consenting adults such as SS would need consideration of sedative medication, covert administration of medication and where physical restraint was needed, this should be done by specialist trained staff. He also postulated possible vaccine risks including general side effects from the injection but including delirium given her dementia. Also considered was how SS may respond herself behaviourally to this and the potential use for short term benzodiazepines for any associated agitation. Any plan involving restraint from care staff would likely be distressing for both them and SS.

The court gave consideration of a relative's well-intentioned suggestion that given SS held the delusion her deceased parents were still alive, it could be suggested to her that her father requested she take the vaccine in the hope she would comply. In considering this, the judgment opined that apart from 'compromising all involved' such 'collusion to trick SS into complying' with the vaccination was on balance something unlikely SS would have wanted whilst capacitous and was 'consistently and volubly opposed' when incapacitous. The judgment noted the relative's instinctive view that such 'means might justify the end' risked compromising SS's 'dignity and suborning her autonomy' and hence could not be in her best interests. The court citied case law from the Supreme Court[4] to buttress its approach: "…in considering the best interests of this particular patient at this particular time, decision-makers must look at his welfare in the widest sense, not just medical but social and psychological".

Conclusion

There was a good case to be made for SS having the vaccine were the judge to 'confine the issue solely' to health-related states, pandemic events and wider Covid-19 data. However, in applying case law as above, a determination of SS's 'best interests' should 'not be confined to the epidemiological' and 'required evaluating welfare in the broader sense'. It necessitated the court to put themselves in the place of the individual concerned. While SS's reality was 'undoubtedly delusional', it did not stop it being her reality, and had to be both recognised and respected. On the basis of the available evidence the judge considered there was 'substantial material from which to conclude' that if she were capacitous, SS would most likely have declined the vaccination. Hence it was not in her best interests to be vaccinated.

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4. *Aintree University Hospital NHS Trust v James* [2013] UKSC 67

*these judgments can be accessed in full for free via the British and Irish Information Institute website: www.bailii.org

Validity of an advance decision in the case of a Jehovah's Witness

by

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Introduction

This article reviews a decision from the Court of Protection[1] regarding the validity of an advance decision (AD) in an older person who was a Jehovah's Witness.

Background

PW is an 80 year old female with Alzheimer's dementia. She presented with severe haematemesis needing admission onto a surgical ward. Investigations revealed an ulcerated Gastro-intestinal stromal tumour (GIST) in the fundus of her stomach causing bleeding. PW's haemoglobin on admission was 8.7g/dl and fell to 5.0g/dl which would ordinarily warrant a blood transfusion.

PW had been a Jehovah's Witness for many years (attending meetings prior to the court case). This religious community are well-known to decline blood transfusions, not only due to risk but due to biblical text. Hence, many Jehovah's Witnesses will carry an AD to refuse treatment specifically regarding administration of whole blood and primary blood components. PW made an AD in 2001 refusing blood products under any circumstances (although made prior to the MCA, the court found it to be still valid and applicable to the decision at hand). Once it was known PW was a Jehovah's Witness haematology advice was sought who advised alternative supportive measures including EPO and iron. A consultant surgeon advised there was an urgent need for blood transfusion.

Due to the severity of the anaemia and potential fatal outcome, the topic of blood transfusion was broached by two separate consultant geriatricians. Dr C initially spoke with PW and recorded that she had declined transfusion but was unsure about whether she had capacity to do so. A separate assessment by Dr J noted

PW could not recall previous conversations about blood transfusions. But when he asked whether she would consent to a blood transfusion if not having it would mean death she replied: *'In that case I would have it, if it was clean blood'.* Thirty minutes later she replied differently: *'In that case, I'll die*' *and 'I have made my peace with Jehovah and will talk to him then.'* Dr J felt, whilst acknowledging fluctuation in capacity, PW did have capacity to refuse a blood transfusion even in a life threatening situation having given a rationale for refusing treatment and understanding consequences. Later, he reflected that PW was unable to give reasons behind her responses and that her answers seemed formulaic and inconsistent. Dr J had not seen the AD when he saw PW. She did not mention it at any stage, nor did she tell him she was a Jehovah's Witness.

Due to inconsistencies between the patient's initial consent to transfusion and her AD, and to issues around PW's capacity to consent/refuse treatment, the case was brought before the court. The issues to decide were:

1. Did PW have capacity to refuse or consent to blood transfusion?
2. If she lacked capacity was her AD to refuse treatment valid?
3. If it was not valid, was it in her best interests to be given a blood transfusion?

The urgency of the 'compelling' need for a transfusion was evident such that clinicians were 'standing by' ready to give blood if authorised by the court.

Capacity

The court concluded on the balance of probabilities, PW, due to dementia, lacked capacity to consent/refuse a transfusion – she was unable to retain relevant information; did not understand the nature and seriousness of her condition which needed a transfusion, and could not use or weigh relevant information.

Advance decision to refuse treatment (s24-26 MCA)

An AD to refuse treatment is a decision made by a person when they have capacity. It is used so that, if a specific treatment is proposed at a time the patient lacks capacity, then that treatment is not undertaken. In regard to life-sustaining treatments, ADs must be written, signed, witnessed and explicitly state that the refusal is for specific treatment(s) even if life is at risk (s25(5)).

Under s25(2) ADs are invalid if:

a) It has been withdrawn by the person at a time when they had capacity to do so.
b) A subsequent LPA authorises a donee(s) to give/refuse consent to treatment to which the AD relates.
c) The person has done anything else clearly inconsistent with the AD remaining their fixed decision (the key issue in this case).

The judgment outlined various 'matters' indicating whether PW had acted inconsistently with the AD remaining her fixed decision:

1. In the 20 years of the AD being in place, whilst she had not withdrawn or revoked it, she had not updated it.
2. PW's family were unaware of the existence of the AD let alone any contents contained therein (the judge noted 'hostility' and 'disdain' of the family towards the Jehovah's Witness faith and hence PW may have been aware of this and been 'dissuaded' from telling them).
3. In the year prior, PW had given LPA for health and welfare to her four children – empowering them to make all decisions on her behalf about her health and welfare, except for refusal or consent to life sustaining treatment. She did not reference her AD, nor request them to refuse blood transfusion or blood products on her behalf or set out similar preferences or instructions under the LPA. The judgment noted that blood transfusion or blood products may be used for treatments other than to sustain life. The AD related to the use of allogeneic blood and blood components for any purpose. The judgment felt this did not appear to be her decision when she made the LPA and hence the granting of the LPA was inconsistent with the AD remaining PW's fixed decision.
4. Her family reported that when PW signed her LPA she told them she wished to be resuscitated if necessary. She did so again without referencing her AD.
5. Earlier in 2021 PW wished for a DNR notice to be removed and did not qualify this by insisting she should not receive a transfusion as part of any resuscitation.
6. The conflicting conversation Dr J had with PW indicated in the first discussion she 'appeared to engage in a form of thought process, avoiding

formulaic language. In the second she seemed to resort to formulaic language and not to be engaged in any form of thought process.'

7. Whilst PW was found to lack capacity to refuse/consent to a blood transfusion, the court was satisfied she was still able to express her wishes and feelings about such treatment 'albeit inconsistently' and at times resorting to 'formulaic expressions'.
8. Because he had the benefit of speaking directly to PW, the court gave weight to Dr J's opinion that he did 'not believe that she genuinely still believes in what she wrote many years ago' in her AD.

Whilst the judge recognised the evidence did 'not all go one way', he was satisfied, on the balance of probabilities, that PW had 'done things clearly inconsistent with the AD remaining her fixed decision' and that pursuant to s25(2)(c) the AD was not valid.

Best interests

In putting himself in 'her shoes', and considering PW's 'welfare from the widest perspective', the judge concluded it was in PW's best interests to receive blood transfusions to restore and maintain her haemoglobin at 10 g/dl – due to the treatment being minimally invasive, very urgent and the consequence of not having it being death.

This case highlights the intricacies involved in ADs. It is important to know the background of any AD as well as the views of the family and whether the patient has shown any inconsistencies with their AD. Doing so will allow clinicians to ascertain whether an AD is valid before using it to withhold potentially life-saving treatment.

References

1. *Re PW (Jehovah's Witness: Validity of Advance Decision)* [2021] EWCOP 52 (22 September 2021)

*the full judgment for the above case can be accessed for free via: www.bailii.org.

Triage: a barrier or a tool for achieving the NHS long term plan of integrated care?

by

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Introduction

The NHS turned the spotlight on the interface between community mental health services and primary care in its Long Term Plan in 2019 [1]. The plan outlines ambitious aims for boundaries between primary and secondary care to be removed for people who are severely mentally ill, including removal of long referral processes where a high proportion of referrals are rejected by mental health services [2]. There is a question whether community mental health (CMH) triage processes serve to perpetuate an outdated "silo" model of care, or whether the triage process could be used to facilitate the desired seamless transitions.

I conducted a survey of the triage process used by an Older Persons' Community Mental Health Team (an organic and functional service for people over the age of 65) based in Gateshead, England. The service holds a daily triage meeting, led by community mental health nurses, that allocates referrals to one or more teams within the service and defines the level of urgency. At the time of the survey, there was no formal referral criteria nor pro forma, and as such the quality and method of referral was varied.

Between 4 Jan 2021 and 26 Feb 2021, the service received 155 referrals, the majority of which were from GPs (74%). Other referral sources included Older Persons' Mental Health Liaison team (17%), Older Adults Crisis Resolution and Home Treatment team (5%), Neurology physicians (3%), and Working Age Adult Services (1%).

Results

Broadly, 79% of 155 referrals received were for cognitive complaints, as opposed to functional presentations, with a quarter of cognitive referrals having a pre-existing diagnosis of dementia.

Over half of patients, 60%, were triaged as requiring psychiatrist review, and 47% of patients were assigned to the CMH nursing team. Referrals were less often directed toward Occupational Therapy (13%) and secondary Psychological services (3%). Only one referral was directed toward each of: the Specialist Memory Hub (a post diagnostic service for people with dementia), Care Home Liaison, and the Younger Persons' Dementia services.

Sixteen percent of referrals received were marked as urgent by the referrer, and following the triage process this increased to 20%. At this time, "urgent" was defined as needing to be seen within 14 days or less. In total, nine (6%) referrals were rejected; seven (5%) referrals were downgraded in urgency; and fourteen (9%) referrals were upgraded in urgency.

Limitations

Over half of the referrals that were upgraded in urgency were received from other secondary mental health services, including crisis and liaison teams. On exploring how these referrals were received, it appeared likely that the urgency was stated verbally by telephone and this had not been captured by the records surveyed.

Discussion

One aim of the NHS Long Term Plan is to optimise information sharing, by way of interoperability between IT systems and shared care records. The Gateshead CMH team shares the electronic note system EMIS with local GPs. This survey has highlighted that the service is not making best use of this asset, which is reflected in a number of referrals having to be rejected as the uploaded documents were either irrelevant, out-dated, or insufficiently detailed to allow triage.

The solution proposed was for an electronic referral Pro Forma to be developed to ensure future referrals are standardised and contain a minimum of information on presenting symptoms, risks, and urgency. The new form also reminds referrers of

baseline investigations recommended by NICE in the investigation of cognitive impairment in particular. Ideally, the Pro Forma, which is in the process of being implemented, will be automatically populated with information from the electronic record, saving time and improving the accuracy of information communicated between services.

Arguably, some may view this as a step in the wrong direction, creating another barrier by way of yet another referral form. However the survey demonstrated there remains a gap in primary care knowledge regarding serious mental illness. Six GP referrals, initially referred as routine, described concerning clinical features that led to an upgrade in urgency at triage. Features included multiple risk factors for suicide, hazardous use of domestic appliances, and physical aggression toward others. One referral was rejected as it was inappropriate for mental health services due to the presenting complaint being motor symptoms of Parkinson's disease.

The triage process has an existing feedback process in place to communicate the rationale for rejected referrals. This this could be further developed to provide feedback on referrals where the urgency has been down or up graded, which would support the upskilling of our primary care colleagues' in identifying risks in those with severe mental illness, a step that has been recognised as necessary in moving toward integrated care in the Long Term Plan.

One of the challenges of moving toward an integrated care system is identifying the work force who will deliver the new model of care. It has been proposed this could be achieved by better use of allied health care professionals and third sector organisations. Locally, this could be implemented by using the triage process to sign post service users to a wider range of services, including peer support or voluntary organisations. At the same time, there is a drive to adopt a single assessor approach, avoiding pathways that necessitate service users to repeat their stories. The survey reveals that the majority of patients in the Gateshead CMH team are seen initially by either a psychiatrist or member of nursing staff. It remains to be seen whether these initial assessments could be allocated to other allied professionals to optimise utility of precious staff resources, preparing ourselves for the demands of future integrated working, or whether this would risk further fragmenting the patient's journey through the care system.

Three of the rejected referrals were for service users who were either under the age of 65 years, or over 65 years and already open to working age adult services. This raises the question of how we best serve the population at the boundary of older age, aiming for an ageless service, without compromising our expertise in older age and frailty, whilst avoiding creating more barriers to patient's accessing care.

Conclusion

The survey has provided valuable insights in to the volume and nature of referrals received by our local particular CMH team. These insights are particularly meaningful when thinking how a future Integrated Care System (ICS) could be tailored to meet our local population's needs, something Dr Amanda Thompsell, National Speciality Advisor for Older Adults' Mental Health at NHSE & I, emphasized as the key to successful ICS proposals during an April 2021 RCPsych webinar on Community Mental Health Transformation [3].

It is my opinion that the triage process has the potential to be a powerful tool in integrating services going forward, and not a barrier. However achieving this potential would require time, skilled staff, and effective IT systems to deliver. These are resources whose scarcity have been identified as a significant challenge in delivering the NHS Long Term Plan as a whole.

I plan to survey the triage process again once the new pro forma is in place; I would like to expand the project to seek the opinions of our GP colleagues.

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Reflections on RCPsych Leadership and Management Scheme: trainee and clinical supervisor perspectives

by

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Dr Patrick Chance, Consultant in Old Age Liaison Psychiatry & Clinical Director OAMH, Aneurin Bevan University Health Board.

Trainees Perspective

I was fortunate enough to gain a place on the 2020/2021 cohort of RCPsych Leadership and Management Fellowship sponsored by Aneurin Bevan University Health Board. I have always held a special interest in Leadership and Management and am currently completing an MSc in Strategic Leadership in Healthcare.

The scheme initially caught my eye as an opportunity to put the theoretical underpinnings from my MSc into practice. The fellowship provides a combination of national teaching as well as a local apprenticeship model within a trainee's health board. This meant I had the opportunity for experimental learning. This is something that can be hard to find during higher training and so I leapt at this opportunity. National teaching was adapted to take place over Zoom in response to the pandemic and used around 10 days of study leave. I used my special interest time to complete a local leadership project over the course of around 9 months.

Learning about leadership during training can often be viewed as an optional extra despite the GMC describing it as a core skill within their Generic Capabilities Framework. However, mental health services for Older Adults currently face unprecedented demand. Trainees need to develop leadership skills to allow them to understand, adapt and overcome to ever changing challenges within both health and social care.

The fellowship scheme was made up of a diverse collection of trainees from different subspecialties across all four nations. This created a community of learning where we could come together, share and learn from fellow's experiences of both success and failure in their local projects. This peer learning became a real source of support and opened my eyes to wider perspectives that I may not have previously considered.

One of the huge advantages of this scheme is the opportunity to be mentored through a leadership project by local leaders. I was fortunate to be mentored by two senior leaders while completing a review of Liaison services. The prospect of such a large project was daunting having previously only completed small QI or audit projects. However, my mentors helped me unpick through complex multi-speciality systems to begin to implement service level change within our organisation.

As a result of this scheme, I am much more aware of my leadership capabilities as a higher trainee. I am more confident in my fledgling leadership skills and feel confident that I will continue to develop these skills as a new consultant. I have developed a network of likeminded peers across the country through the Leadership Fellowship alumni which will continue to provide me with a reflective learning space to further develop as a leader. I also feel the organisation have benefited from this scheme; from investing in emerging leaders and completion of a project to improve patient care. I would urge other health boards to invest in their Older Adult Higher Trainees as emerging leaders and consider sponsorship on this scheme.

Clinical Supervisor Perspective

In 2020/21 ABUHB sponsored my ST5 trainee, Dr Jen Rankin, to successfully gain a place on the RCPsych Leadership and Management Fellowship.

She came to work with me for one year in Old Age Liaison Psychiatry already having developed a special interest in Leadership and Management and was undertaking an MSc in Strategic Leadership in Healthcare, so enrolment on the RCPsych Fellowship seemed an obvious complementary and development opportunity not to be missed.

We were able to incorporate the central teaching sessions into her study leave allowance and used timetabled special interest time to allow her to develop and complete a local leadership and service improvement project during the course the year. Having Clinical Director managerial responsibility allowed me to provide insight and guidance to how she should approach her project.

Leadership has long been part of training curriculum for higher trainees in psychiatry but finding formal opportunities to develop these skills and competencies has been a challenge. Reflecting on my own experience of higher training some 15-16 years ago, leadership and management training opportunities were very much ad-hoc and sporadic. When I completed my CCT in General Adult and Old Age Psychiatry in 2007, I felt well prepared for the clinical challenges of working as a consultant psychiatrist but my management knowledge and leadership skills were relatively superficial. It then took me the best part of 10 years working as a consultant, learning on the job, to be able to successfully apply for a senior leadership and management role as Clinical Director for OAMH.

Complementing the clinical placement in old age liaison psychiatry the project that we helped Dr Rankin identify was a review of general adult liaison services within the health board with the aim of going on to develop a business case to provide a more multidisciplinary and comprehensive general adult liaison service beyond the existing nurse-led deliberate self-harm assessment team.

To support Dr Rankin in the project we established a supervising steering group made up of myself as her clinical supervisor, the Divisional Director for Mental Health & Learning Disabilities (MHLD) in ABUHB, Divisional MHLD Lead Nurse and also administrative support from our divisional medical staffing coordinator who was herself looking to develop project management skills. This steering group met on 6-8 weekly basis to review work done and provide guidance on next steps.

Development of a more comprehensive psychiatric liaison service for patients of working age has been an Integrated Medium Term Plan (IMTP) priority area for the MHLD Division for the last 3-4 years following previous successful development of an old age psychiatric liaison service in 2014-16. However progressing this IMTP priority has proved difficult without dedicated clinical leadership time focussing on general adult liaison psychiatry needs. Having the committed and protected clinical leadership time from an RCPsych fellow, for a whole year, has given that

needed focus and impetus to complete a formal review of the existing service which in turn has put the MHLD Division in a stronger position to bid for any new liaison psychiatry service-improvement funding that may arise.

Over the course of the year, I observed Dr Rankin grow in her leadership and management skills and confidence. Now in her final ST6 year as an old age psychiatry trainee, I am confident that Dr Rankin will be an excellent position to apply for a consultant psychiatrist post and will have the acumen and skills to become involved in any arising leadership and management challenges and opportunities.

A.R.T.S. for Brain Health – Social Prescribing as Peri-Diagnostic Practice for Dementia: From Despair to Desire

by

Veronica Franklin Gould, President, Arts 4 Dementia

On World Alzheimer's Day, 23 September 2021, Arts 4 Dementia published the first report on social prescribing (SP) as peri-diagnostic practice for dementia, discussing referral to weekly arts at the onset of symptoms, to provide support and help combat fear and isolation in the period leading to memory assessment and diagnosis. The report outlines cross sector process and partnerships for sustainable programming.

Dementia prevalence and Brain Health

Each year, there are over 200,000 new cases of dementia in the UK. One-third more will not receive a diagnosis, either due to personal or cultural fears. As our most feared condition, progressive degeneration of the brain, its name 'dementia' itself and associated stigma is a deterrent; and of those referred for memory assessment, one-third will not have a dementia diagnosis.[1] There is currently no available cure, no vaccination, and until diagnosis, no support. All would derive cognitive benefit and enhanced wellbeing at the outset of symptoms, through participating in arts programmes to preserve their brain health.

Why A.R.T.S.?

Engaging in social A.R.T.S. (wide-ranging **A**ctivities to **R**evitalise **T**he **S**oul) empowers individuals to address modifiable risk factors for dementia, combat stress, reduce isolation, preserve their sense of identity, of purpose, or belonging, so that peri- and post-diagnosis, their resilience in the community can continue, for years longer.

Everyone, according to the Universal Declaration of Human Rights, (1948, Article 27), has the right freely to participate in the cultural life of the community. Whereas referral to A.R.T.S. support for dementia has required diagnosis, GPs can now at the onset of symptoms refer them to their practice SP link worker (SPLW) for arts prescription.

What is social prescribing?

SP, a key component of NHS Universal Personalised Care, enables GPs, memory services and local agencies to refer people to an SPLW for non-clinical sources of support for their wellbeing to empower them to take greater control of their own health.

A.R.T.S. for Brain Health - Social prescribing transforming the diagnostic narrative for dementia from despair to desire

The report, informed by 400 speakers at A4D's two national conferences and 15 regional cross-sector meetings throughout the UK, leaders in dementia prevention, creative ageing, SP, culture, health and wellbeing, people with lived experience, GPs, memory services and local authorities, examines

- How engaging in A.R.T.S addresses modifiable risk factors for dementia and protects against the advance of cognitive decline.
- Current diagnostic practice for dementia, with case studies from patients, how GPs and memory services offer or plan to offer SP.
- SP, creative ageing and A.R.T.S. for brain health, with case studies.
- Models for collaborative practice, for arts organisations to raise awareness to SPLW and achieve sustainable A.R.T.S. programmes.

Preventing well – A.R.T.S. modifying risk factors

As one-third of cases of dementia could be prevented, risk factors and how A.R.T.S. protect against the advance of dementia are examined.

1. Learning vs lack of education: Learning music, poetry or drama, exploring works of art, discovering the artist's intention, challenges the brain to create new neural connections and pathways that can compensate for reduced activity in other regions. Opening the door to new discovery and engaging interest is the essence of cognitively stimulating A.R.T.S. workshop programmes run through arts organisations' learning or community teams,

as well as community arts hubs or healthy living centres. Co-curating A.R.T.S. programmes heightens sense of identity, purpose and connectivity as members of a resilient, socially active group.

2. Social contact vs loneliness and isolation: Social connectivity involved in person-centred A.R.T.S. plays a vital role protecting people at this vulnerable cusp, across all social backgrounds and cultural ethnicities. A.R.T.S. fulfil their core psychological need, nurture social bonding, personal identity through collaborating in creative endeavour.[3]
3. Dance movement vs physical inactivity, obesity and depression: Dance offers a joyous route to health and wellbeing, more effective than an exercise class in reducing body fat, fall prevention and, through the role of music, in improving mood, reducing stress and helping to maintain attention. Learning new steps, to lead and follow, enhances hand-eye coordination.[4]
4. Music vs depression: As we age, music-making provides a tool for a total brain workout, improves plasticity in the cortex, which enhances the ageing brain's cognitive abilities – perception, motor function, working memory – improves cardio-vascular strength. It allows creative self-expression, reducing stress and giving a joyful sense of accomplishment.[5]
5. Connecting actively with nature vs physical inactivity: Group activities for wellbeing and camaraderie in nature help protect against obesity, sleep deprivation, anxiety, depression and social isolation.

Diagnosing well – The patient journey

According to GPs, it takes several years from the start of symptoms to get a dementia diagnosis and the wait for a memory assessment appointment can be three to fourteen weeks, or more. Memory services who hitherto proposed arts as post diagnostic support now advise patients awaiting appointments to take up A.R.T.S. as now suggested in Dementia Change Action Network's Next Steps website.

Supporting well – social prescription

Introduced through the NHS Long Term Plan in 2019, there are now 1,500 SPLW around the UK available to every GP and local agencies who can now refer patients to their SPLW for non-clinical, psychosocial sources of support, such as A.R.T.S.,

whatever is of greatest interest to the patient. If it doesn't exist locally, SPLW, who are trained and supported by the Social Prescribing Network's regional learning coordinators, may have access to a community builder who can help support its set up.

Living Well – A.R.T.S. to preserve brain health

Referring patients for arts prescription at the onset of symptoms reduces anxiety, preserving resilience for the individual and their partner together in the community. The report highlights A.R.T.S. practice for brain health as weekly participatory activities, challenging but achievable, designed to re-energise and inspire, with arts teams trained in early-stage dementia, understanding the challenges people face as early symptoms of mild cognitive impairment and the various dementia subtypes arise. There is no sense of dementia here – except that it is understood and if a diagnosis is confirmed, participants remain part of the group, co-curating, improvising, inspiring each other, as regional case studies and the A4D web-listing for brain health and for dementia illustrate.

ArtsPAL

To enable individuals to access A.R.T.S. prescription programmes, and accompany them in creative endeavour, A4D has set up a cultural and creative befriender network ArtsPAL, by region.

The Way Forward

For sustainable A.R.T.S. programmes, the report highlights the National Academy for Social Prescribing (NASP)'s place-based Thriving Communities Fund, a cross sector, partnership model, ideal to raise awareness and funding and enables sustainable A.R.T.S. programmes.

The World Health Innovation Summit has agreed to fundraise to further this programme, in particular, longitudinal academic research, starting in September 2022.

The report proposes an amendment to the NICE guideline 97 for Dementia, 1.2 Diagnosis: Initial assessment in non-specialist settings, page 15: to insert before 1.26 a recommendation to SP for brain health.

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Reflections as a Trainee Rep in changing times

by

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Dr Orima Kamalu, ST6 Dual OA/GA Trainee, Severn Deanery

Earlier today, Manny and I closed the final session of the biggest RCPsych Trainee Conference to date at the inaugural RCPsych Old Age Psychiatry Trainees Conference, and announced the names of the two new trainees who we have elected to take over our roles as the Old Age Faculty Higher Trainee Representatives. This feels like the perfect moment to reflect on our time in the role and take stock of what we have achieved.

Manny began his "term in office" back in late 2019 and hit the ground running attending College faculty meetings and launching into preparations for the Trainee Day at the full RCPsych Faculty of Old Age Psychiatry Annual Conference which was initially scheduled for March 2020, but was of course cancelled for reasons that will be familiar with us all now.

I was fortunate enough to be elected into the role in September 2020, after the previous co-rep, Dr Chloe Pickup, stepped back after two years working in the role. It was initially daunting as a trainee to join virtual meetings with the group of renowned senior clinicians, academics and leaders from all around the country that comprised the Executive Committee, but Manny and I were always made to feel like a very welcome and integral part of the team, whose voices as trainees were a vital part of any discussion. Undeterred by the pandemic, the Executives pressed hard to reorganise and deliver the Faculty of Old Age Psychiatry Annual Conference, albeit online, and in March 2021, they ran what ended up being the largest RCPsych sub-faculty conference to date. On the back of this, Manny and I were greatly encouraged by our faculty colleagues to resume plans for a Trainees Conference, but as a stand-alone day with a unique focus on education and training.

Lucky for me, Manny had already done most of the groundwork in preparing and inviting speakers to the formerly planned event, so there was already a solid foundation of ideas for the new programme. However, this had been an unprecedented year for trainees, clinically, educationally and emotionally, and the changes to healthcare provision and needs both related and not related to COVID meant there were many additional avenues and opportunities for discussion at the new event.

The final programme covered four themes across four sessions in the day: 'Education, Training & Wellbeing', 'Trainee Presentations', 'Subspecialties in Old Age Psychiatry' and 'The Future of Old Age Psychiatry'. We were honoured to have invitations accepted to speak from clinicians, academics and leaders from all career stages, from the Dean of the College, Prof. Subodh Dave and National Specialty Advisor, Dr Amanda Thompsell, to fellow trainees from Foundation Doctor to Higher Trainee level.

Some of the highlights from the morning included a keynote from the Dean on his visions in the role, and an update on the new RCPsych Curricula. Talks on trainee wellbeing and support were followed by three fantastic oral presentations from trainees at different career stages. All three trainees were awarded a prize and complimentary attendance at the Faculty of Old Age Psychiatry Annual Conference 2022 due to the outstanding level of their presentations. The afternoon 'Subspecialties in Old Age Psychiatry' session demonstrated the wide variety of clinical and academic opportunities within our specialty. A major highlight was the session 'Are we ready for disease modifying treatments?' which yielded considerable discussion between the panel of experts and trainees via the chat and Q&A functions. The final sessions highlighted upcoming changes to the Mental Health Act and community mental health provision.

One of the biggest challenges as a trainee representative this year was the continued restrictions due to COVID-19 and the emphasis on continuing to work remotely and hold events virtually. Even Manny and I worked together throughout from opposite sides of the country! I feel this meant that although we were able to join faculty meetings online with relative ease, our ability to connect physically with Old Age trainees around the country as a representative was somewhat hampered. However, we were delighted to discover in the days leading up to today's event that a record breaking (for a sub faculty trainee conference!) 180

people had registered to attend, comprising of mainly core and higher trainees, but also a number of medical students, foundation doctors and consultants, too. I hope that through hosting such a successful conference, we succeeded in bringing our junior colleagues together, albeit virtually, on a platform specifically dedicated to the needs and interests of trainees.

Our final piece of work before we leave the post is to contribute to the planned changes to the training curriculum that will be coming into place next year via attendance at the Specialty Advisor Committee meetings and through development and publication of example Old Age Psychiatry Personal Development Plans. These are planned to be used as frameworks to plan one's training journey, check off competencies alongside the curriculum and directly feed into our placement sign-offs for ARCP.

At the end of today's conference, we introduced the two new trainees who will be taking over from us as higher trainee representatives, Dr Funmi Deinde (ST6, SLaM) and Dr Lizzie Robertson (ST4, NHS Lothian). They, too, will be spanning the country (albeit in a different plane!) but we are confident given their individual skillsets and passion for training that they will continue to build upon the work we and our predecessors have done in the role, and continue to ensure that Old Age Psychiatry remains the greatest training programme one could possibly choose!

Cochrane Corner

by

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Featured reviews:

- Multi-domain interventions for the prevention of dementia and cognitive decline
- Anticholinergic burden (prognostic factor) for prediction of dementia or cognitive decline in older adults with no known cognitive syndrome.

The estimate that 40% of dementia may be preventable by modifying known risk factors is widely cited[1]. In a recently published review, Hafdi and colleagues[2] set out to assess some of the research which has been done to date to try to translate this hope into practice (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013572.pub2/full). They argue that, since sporadic dementia is a complex condition with multiple causes and risk factors, it is likely that complex interventions which target more than one risk factor will be more effective than simple interventions which target a single factor. Therefore they focus their review on RCTs of 'multidomain' interventions (interventions with two or more components targeting different risk factors) applied to populations aged 50+. The study populations could be unselected or selected on the basis of increased dementia risk. Eligible studies had to include at least 400 participants and had to follow them up for at least 12 months. The primary outcomes in the review were incidence of dementia or MCI, cognitive decline and mortality.

Searching up to April 2021, the authors found nine completed RCTs with 18,452 participants; they also identified eight ongoing trials, demonstrating the level of research activity in this area. The interventions studied were diverse. The domains targetted in one or more of the included trials were: diet, physical activity, weight loss, blood pressure control, diabetes management, blood lipids, smoking, alcohol

intake, cognitive training, social activities and self-management of risk factors. (The latter was part of all the included interventions).

Only two studies (7,256 participants) assessed the incidence of dementia. Follow-up times in these two studies were 6-8 and 10-13 years. It is well worth reading the review to understand the nature of the studies (populations and interventions) in more detail, but the headline is that there was little or no effect on dementia incidence. The incident rate was 4% in both the intervention and control groups and the pooled relative risk (RR) was 0.94, 95% CI 0.76 to 1.18. The longer of these two studies was the only study to assess incidence of MCI and there was probably no effect on this outcome either (RR 0.97, 95% CI 0.76 to 1.23, 3802 participants). There was, however, a small benefit of multidomain interventions on cognitive function measured with a neuropsychological test battery (MD in composite z-score 0.03, 95% CI 0.01 to 0.06; 3 studies; 4617 participants) and also, although with very low certainty, on cognition assessed with the MoCA. There was no evidence of an effect on cognition assessed with the MMSE.

The authors looked for, but did not find, evidence of an interaction of the effects of multidomain interventions with baseline cognitive function or with a vascular risk score. However, they did find evidence that multidomain interventions may be more beneficial for cognitive function in carriers of the apoE4 allele. They also comment that the effects on cognitive function were greatest in the trials which included a cognitive training component, and have some concern that it could reflect a training effect.

These are obviously very challenging trials to do, needing large samples and long periods of follow up. But given the magnitude of the public health problem presented by dementia, the rewards for success would be great and this will definitely be a fascinating field of research to watch in coming years. The authors complete their review with a stimulating discussion of the implications of their findings for future research.

One possible modifiable risk factor for cognitive decline which was not addressed in any of the trials in Hafdi *et al*'s review is anticholinergic burden (AChB, i.e. the overall anticholinergic effect of all the drugs a person is taking). NICE's 2018 dementia guideline recommends considering anticholinergic burden as a factor that may be contributing to cognitive impairment and suggests using a validated scale to measure it. But how robust is the evidence that AChB is a risk factor for

dementia or cognitive decline? Taylor-Rowan *et al* [3] used methods developed for synthesising data from prognostic factor studies to address this question in their review *Anticholinergic burden for prediction of dementia or cognitive decline in older adults with no known cognitive syndrome* (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013540.pub2/full). Given the diversity of scales in the literature which purport to assess AChB, the authors also hoped to be able to compare the prognostic validity of different scales for predicting cognitive decline, and hence to help clinicians to decide which (if any) scale to use.

Eligible studies were prospective and retrospective longitudinal cohort and case-control studies with a minimum of one year' follow-up that examined the association between an AChB measurement scale and future cognitive decline or dementia in cognitively unimpaired older adults. Twenty-five such studies, including 968,428 older adults, were identified up to March 2021. Risks of bias in the included studies were high. The most common bias issues were absence of methods to exclude reverse causation (14 studies at high risk of bias), missing data (nine studies at high risk of bias), and studying specific populations so that the results may not be generalisable (nine studies at high risk of bias). Although most studies controlled for age, sex and medical comorbidities, half did not control for psychiatric comorbidities such as depression.

Twenty-three of the 25 studies reported a significant association between anticholinergic use and increased risk of any type of cognitive impairment: 9/11 reported a significant increase in risk of dementia; 3/3 in risk of dementia and MCI combined; 1 /4 in risk of MCI only; 12/14 in risk of reduced performance on a wide variety of cognitive tests. Unfortunately, there were sufficient data on only one scale – the Anticholinergic Cognitive Burden scale (http://www.agingbraincare.org/tools/abc-anticholinergic-cognitive-burden-scale) - for 'scale-based' meta-analysis and too few data for any meaningful comparison between scales. Pooling fully adjusted odds ratios, there was an increased risk for cognitive decline or dementia in older adults with an anticholinergic burden on the Anticholinergic Cognitive Burden Scale (OR 2.63, 95% CI 1.09 to 6.29). A similar result was found in an exploratory analysis which pooled results across different scales. The authors considered the overall quality of the evidence to be low because of the risks of bias, the imprecision of the estimate and the risk of publication bias. However, there was evidence of a

correlation between the severity of the AChB and the magnitude of the risk of cognitive decline or dementia, which increased confidence in the result.

The balance of the observational evidence, therefore, is clearly in favour of AChB being a risk factor for cognitive decline, but the evidence is incomplete and subject to multiple biases. The proof of the pudding will, of course, lie in intervention studies and the same authors are planning a review of trials which have sought to assess the effect on cognition of interventions to reduce AChB. It may be possible to detect effects on cognitive function, although as Hafdi and colleagues argued in their review of preventive interventions, finding an effect on dementia incidence from an intervention in a single risk domain may be unlikely. For now, it would seem sensible to follow the advice to attend to anticholinergic drug burden in clinic and to consider use of the Anticholinergic Cognitive Burden scale as the best evidenced scale for this purpose.

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Research update

by

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Brown *et al*. Frailty Worsens Antidepressant Treatment Outcomes in Late Life Depression.[1]

Previous research has shown that late life depression (LLD) is associated with worse treatment outcomes and higher recurrence rates when compared to younger adults. In addition, frailty has been shown to have a bidirectional relationship with LLD and is associated with increased mortality risk. The aim of this study was to explore the relationship between frailty and the response to antidepressant treatment in adults with LLD. The study participants were selected from patients seen at the Clinic for Aging, Anxiety, and Mood Disorders at the New York State Psychiatric Institute between June 2013 and December 2018.

A total of 100 participants aged over 60 years were included in the study. Each participant had a diagnosis of either major depressive disorder or persistent depressive disorder, and had a rater-administered 24-item Hamilton Depression Rating Scale (HDRS) score of ≥16. Each participant was assessed for frailty by measuring gait speed, grip strength, activity levels, fatigue, and weight loss. Participants were deemed to have frailty if they had ≥3 of these characteristics.

Each participant was treated with an antidepressant (escitalopram or duloxetine) either openly or as part of a placebo-controlled 8 week trial. Each participant was reviewed weekly for 8 weeks. After the 8 week acute trial, participants were given the option of continuing with open-treatment for 10 months, during which there was no treatment protocol and their antidepressants could be switched and augmented as clinically indicated. The trial assessment points were at baseline, 8 weeks, 6 months, and 12 months.

The study found that on average, over the 8 week acute phase, frail participants experienced a significant 2.82 fewer HDRS points of improvement than the non-frail participants, with this difference persisting over 10 months of open-treatment. The study also reported that frail participants had 10-15% lower remission rates compared to the non-frail participants at 8 weeks and 6 months follow up, however this relationship was not statistically significant. They reported that both weak grip strength and low physical activity levels were associated with less improvement on the HDRS. Participants with frailty were treated with more antidepressant medication trials per month compared with non-frail participants.

This study has highlighted that perhaps we, as old age psychiatrists, should be assessing our patients for frailty in order to help inform us about our patients' prognosis and guide our discussions with patients and their relatives. The authors suggest that our frail, depressed patients may benefit more from prompt input from physical therapy teams, behavioural activation strategies and exercise interventions.

Parada *et al*. Dual impairments in visual and hearing acuity and age-related cognitive decline in older adults from the Rancho Bernardo Study of Healthy Aging.[2]

The aim of this longitudinal cohort study was to explore the associations between dual impairments in visual and hearing acuity and age-related cognitive decline. Vision impairment was defined as vision worse than 20/40. Hearing impairment was defined as pure-tone average thresholds >25dB. Participants were adult residents of Rancho Bernardo in San Diego, California. Participants originally had their visual and hearing acuity as well as their cognitive function assessed between 1992 and 1996. The participants underwent repeat cognitive assessment roughly every 4 years thereafter over a maximum of 24 years (mean = 7.3 years). The cognitive assessment included the Mini Mental State Examination (MMSE), the Trail-Making Test Part B (Trails B) of the Halsted Reitan Battery, and the Verbal Fluency Test (VFT).

Out of a total of 1,383 participants, 293 had a visual impairment, 990 had a hearing impairment and 251 had both. The authors used a linear mixed-effects model to examine the associations between the participants' baseline impairments

in visual and hearing acuity and their longitudinal cognitive tests scores. They found that low visual and hearing acuity at baseline was associated with poorer MMSE and Trails B scores. They also found that MMSE, Trails B and VFT scores decreased at a quicker rate in the participants with low visual and low hearing acuity. They also found that low visual acuity was independently associated with poorer MMSE and Trails B test scores but not statistically significant for VFT scores.

A limitation of the study was that they only examined one aspect of visual impairment, focusing on distance vision. This may have impacted on the study outcomes as, interestingly, for those with impairments only in visual acuity, there was no statistically significant decline in VFT scores, the only test that did not require use of vision. Further studies are required to assess the impact of impairment of near vision on cognitive decline.

The study concluded that impairments in both vision and hearing impairments, independently and combined, are associated with a more rapid decline in cognitive function. They highlighted the importance of early identification and management of those with visual and hearing impairments.

Lipsitz *et al*. Safety, Tolerability, and Real-World Effectiveness of Intravenous Ketamine in Older Adults With Treatment-Resistant Depression: A Case Series.[3]

This case series aimed to assess the effectiveness, safety and tolerability of repeat-dose intravenous (IV) ketamine use in a group of older adults (≥60 years) receiving outpatient treatment for treatment resistant depression (TRD) between July 2018 and September 2020. They defined TRD as an insufficient response to ≥2 adequate antidepressant trials. The study used data from an ongoing case series at the Canadian Rapid Treatment Centre of Excellence in a post-hoc analysis.

The study included 53 participants who received a total of 4 IV ketamine infusions over 1-2 weeks. The mean age of participants was 67 years (range = 60-82 years). Among the exclusion criteria were participants who exhibited signs of dementia and those who had unstable or untreated medical conditions such as hypertension or seizures.

They assessed the effectiveness of the IV ketamine using the Quick Inventory for Depressive Symptomatology – Self Report 16 (QIDS-SR16) at baseline, 2 days after infusions 1 to 3, and 1-2 weeks after infusion 4. Safety was measured by assessing for haemodynamic changes before, during, immediately after, and 20 minutes after each infusion. They measured tolerability by the systematic reporting of treatment-emergent adverse events during and after each infusion. They also calculated response rates defined as: partial response, 25-50% symptomatic improvement from baseline; response, ≥50% symptomatic improvement from baseline; clinically significant improvements, ≥25% symptomatic improvement from baseline; and remission rates, QIDS-SR16 ≤5.

The participants reported statistically significant decreases in depressive symptoms with repeated ketamine infusions. The mean QIDS-SR16 score was 17.12 at baseline and decreased to 12.52 after 4 infusions. Following 4 infusions, 31% partially responded to IV ketamine, 27% responded, 58% reported clinically significant improvements, and 10% met remission criteria. Sixty-six percent experienced treatment-emergent hypertension during at least 1 infusion, and 21% required intervention with an antihypertensive. The most commonly reported adverse event was drowsiness (50%), followed by derealisation (41%), and confusion (40%). Three participants discontinued treatment, one after 1 infusion due to worsening anxiety, two after 2 infusions due to dissociative symptoms and worsening anxiety symptoms.

The paper concluded that response and remission rates of the study population were comparable to those previously reported in general adult samples. A cautionary note was made about the associated transient treatment-emergent hypertension in this study population. Limitations include a lack of placebo arm, that participants were prescribed a number of different antidepressants prior to and during the trial, and long term follow up data is not available. This study adds to the emerging real-world data about the safety and tolerability of IV ketamine use however, more research in older adults over 70 years of age is required.

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Book Review

by

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The Old You by Louise Voss

Published: 2017

Publisher: Orenda Books

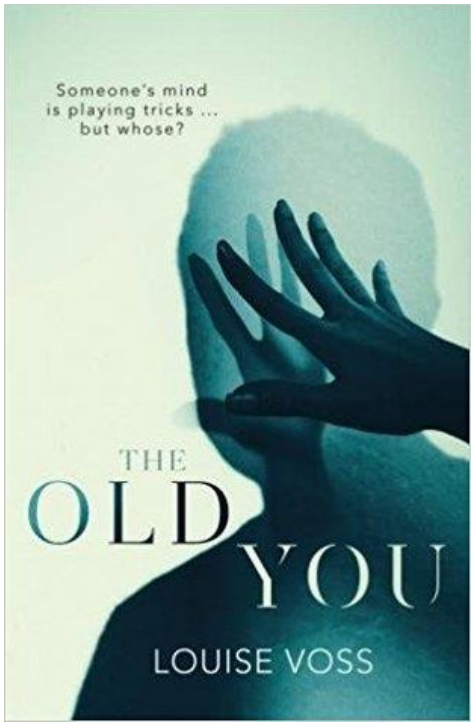

Image from Goodreads

The Old You, by Louise Voss, is a domestic noir thriller with a bit of an old age psychiatry twist. Lynn Naismith has been happily married for the last ten years and is about to start a dream job. But then her husband Ed is diagnosed with young onset dementia and her life changes. As Lynn deals with the fallout from his diagnosis, she finds strange things keeps happening. Is it Ed's mind that is playing tricks, or hers?

Unfortunately, the book starts off inaccurately with a Consultant in a memory clinic making a diagnosis of young-onset dementia without scans or neuropsychology. He also insists on being called Mr Deshmuke instead of Dr which may explain why

his skills in breaking the diagnosis need improvement. Despite this, the author does capture the shock some carers have when their loved ones are unable to complete a simple clockface and when confronted with a life-changing diagnosis.

In the first half of the book, Lynn finds herself coming to terms with how Ed's diagnosis will change her life and the future they dreamed of. She has to manage the change in her husband's personality from the kind, caring husband she fell in love with to a man who is verbally aggressive. She also feels guilty about the annoyance when he is unable to remember his passwords or loses his keys. Things come to a head when he physically attacks her in his sleep and she has to lock him up in his room at night to keep herself safe and sane.

I found these descriptions realistic and found myself empathising with Lynn when her life changes. These are the words I hear so many carers say and we try to manage these with the tools we have available. But these are never enough and so when Ed signs himself for a trial for a miracle trial, you can understand the reasons why.

Anyone who works in old age psychiatry will figure out the 'twist' very quickly but this is still an entertaining read and perhaps one of the few crime thrillers where dementia plays a key role.