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Reflection (284 words)

As an undergraduate neuroscience student, Parkinson's Disease (PD) interested me scientifically: How do the drugs we use work? Why might they cause impulsivity? Why is neurodegeneration so specific to nigrostriatal neurons? These questions drifted in my mind as I was introduced to an 87 year old with PD and depression during my GP placement. Ben's warmth and storytelling ability immediately made me thankful I was not being held to 10 minute appointments, and could lap up Ben's tales of his life and family without being conscious of time. I soon discovered that although open and willing to share about many aspects, Ben was very avoidant when talking about PD. My initial thoughts regarding neuroscience were soon forgotten as I became more interested in how Ben copes psychologically with his diagnosis, and how it affects him socially. This was the beginning of a consultation that taught me much about the holistic needs of patients with chronic disease, as well as how chronic disease can shape our identities. Michael Marmot emphasizes the psychological importance of feeling in control of our own lives¹. A diagnosis of PD can make patients feel they are losing control over the narrative of their lives, and there is a sense that after all those years of life, one has earned authorship over its closing chapters. Ben's avoidant coping struck me as a maladaptive method of regaining control of his narrative. Unfortunately, this also precluded him from engaging with his condition and seeking help to manage the psychosocial aspects of PD. Ben's story inspired me to review the literature around the biopsychosocial aspects of PD and particularly focus on the psychological coping strategies of PD patients, a progressive disease with no disease modifying treatment.

Depression in patients living with Parkinson's disease and its biopsychosocial determinants (3000 words)

Introduction

Parkinson's disease (PD) is a neurodegenerative movement disorder which disproportionately affects the elderly². Rigidity, akinesia and tremor are major motor symptoms of PD². Patients with Parkinson's disease (PwP) also suffer from non-motor side effects of which depression is frequent². Neurochemical hypotheses, including a catecholaminergic deficit in PD may in part explain the high comorbidity of depression and PD³. A systematic review revealed that 17% of PD patients classify for major depressive disorder, whilst 35% have clinically relevant depressive symptoms⁴. Depression in PD (dPD) is consistently ranked as a major determinant of health related quality of life (HrQoL) in PwP⁵⁻⁷. Significant overlap exists between PD and depression, for example both can manifest as lack of motivation and fatigue³. This is important methodologically as it may confound scales used to determine prevalence and severity of dPD⁸. Indeed, some question the validity of studies using generic scales such as Beck's Depression Inventory for PwP⁸, which are common and used throughout this essay. However, more recent validity studies support their use and have given recommendations on which scale to use based on study design^{9,10}.

To appreciate the multifaceted relationship between depression and PD, this essay considers determinants of dPD using the biopsychosocial model. The story of Ben (pseudonym), an 87 year old man with depression and PD is used throughout as a vignette.

Biomedical factors

Management of motor symptoms

Some authors have argued that dPD is linked to the control of motor symptoms¹¹. Indeed, Schrag et al. found that depression was most frequently found in patients just after diagnosis or at a late stage of disease¹². This led them to hypothesize that following the shock of diagnosis, effective management of disease using dopaminergic medications relieves depressive symptoms, before they reappear due to severity of disease becoming unmanageable by treatments¹². However, others have failed to find an association between motor symptoms and depression throughout the course of PD¹³, demonstrating the variability of this link. Reflecting this variability, categorising dPD as relating to motor symptoms or unrelated to motor symptoms has been suggested as part of a management strategy by Timmer et al.¹⁴. They recommend optimisation of treatment of motor symptoms for depression related to motor effects¹⁴. Whilst undoubtedly true, the utility of this distinction is dubious, as, whether or not a patient is depressed, one would hope that regular adjustment and optimisation of treatment for motor function is provided.

Pain

Pain is a dominant issue in managing Ben's condition. Musculoskeletal pain is the most common category of pain in PwP, and is likely caused by rigidity and bradykinesia, although lower pain thresholds mediated by basal ganglia pathology could also be a contributing factor¹⁵. Ben's pain is localised to his lower back and neck and is probably related to his kyphotic posture.

It is widely accepted that pain is associated with depression in the general population¹⁶, and PwP¹⁷. Attempts to establish direction of effect between chronic pain and depression have been inconclusive¹⁸. A bidirectional relationship is therefore most likely. Depression may potentiate pain neurobiologically¹⁹, or via psychological factors such as catastrophizing²⁰. On the other hand pain can drive patients to catastrophize, have low self worth and feel helpless²¹. Indeed, Ben reports greater psychological distress now that his pain has progressed beyond management with topical NSAIDs. Furthermore, neck pain has limited Ben from gardening and playing golf, two activities important to his well-being: 'If I can't go out and play a round of golf, what's the point?'

The bidirectional relationship between pain and depression suggests an integrated treatment approach would improve both outcomes. This is emphasized by evidence showing that persisting pain impedes successful treatment of depression²². Unfortunately, Ben's pain is currently not well managed. A session with a physiotherapist was unproductive and led to frustration for Ben. He was told his PD related posture was the likely cause of his neck pain, but took this to mean he is at fault: 'they were only interested in what *I* was doing and gave no treatment whatsoever'. This negative experience and the fact that depression may impede adherence to physiotherapy²³ have led Ben to not seek further appointments. This should be seen as a failure given physiotherapy is an effective treatment for posture in PD²⁴ and thus is likely to improve Ben's issues with pain. Ben was also trialled on a serotonin-noradrenaline reuptake inhibitor (SNRI). SNRIs such as duloxetine are indicated for chronic pain as well as depression²⁵, and thus may be a good candidate for comorbid pain and depression in PwP²⁶. However, it may be overly reliant on a biomedical model of depression and pain to hypothesize the efficacy of SNRIs for comorbid pain and dPD, as some authors do^{26,27}. One paper wrote that duloxetine might be the 'ideal candidate'²⁸. In fact the evidence base is very weak, with one open label study of 20 patients finding effectiveness for pain in PwP²⁹, a result subject to bias due to lack of randomisation and

small study size. This finding was not repeated in a blinded randomised control of duloxetine in 46 PwP in pain²⁸.

Ben quickly stopped taking his SNRI, citing intolerable side effects on his mood. His rejection of physiotherapy and pharmacotherapy fits into his depressive narrative of helplessness: 'I'm afraid that's just how my life is, nothing ever gets fixed'. This self fulfilling attitude might be common amongst depressed PwP and must be taken into account by providers of care, who should particularly explore underlying reasons for nonadherence to treatment.

Social factors

Friends and family

Social support from friends and family protects against dPD^{30,31} and is a major predictor of HrQoL in PwP⁶. The protectiveness of social support against depression is also found more generally in the elderly population, with spousal support being particularly important for elderly men³². Ben's wife's illness and son's divorce are inherently stressful life events that are likely to have contributed to his depression³³, but these issues have also affected his perceived social support. In the first instance, his role as a caregiver to his wife has increased and in the second, his son's divorce has led to his grandchildren moving away and thus visiting less frequently. Grandchildren are a important source of social support for elderly PwP and their spouses³⁴. Furthermore, it is well documented that spouses acting as informal caregivers can cause stress on the relationship and to the caregiver themselves³⁴. Indeed, Ben notes that he 'doesn't know how she puts up with me'. Social workers tried to support Ben and his wife around the time of her mastectomy, but the couple eventually refused help because the social workers tried to make changes they did not want. For this sort of social support to be most effective, providers must recognise the importance of independence for PwP and spousal caregivers³⁴ and complement this dyad rather than impose upon their way of living. This is best seen in Ben's attitude that 'After 70 years of marriage, we should be the ones looking after each other'.

These issues highlight the need for wider social support beyond immediate family, highlighted by the fact less social support from friends is associated with worse dPD³⁰. Sadly, despite this need, the pattern is usually one of increased social withdrawal from friends and eventual reliance on family as a sole source of social support³⁴. Ben says that he and his wife rarely see friends now, often going weeks without seeing anyone outside of his family. One hypothesis for the benefit of social support is to act as a 'buffer' to stressors³⁵. It is reasonable to expect this to fail if, as in Ben's case, the stressors are traumatic live events happening within the family support group itself, further emphasizing the need for a wider support group which may include friends or community support groups.

These interventions may be an effective way of increasing socialisation for Ben and other PwP, but issues such as the stigma of accepting help are barriers to participation³⁶. NICE guidelines for depression in adults published in 2009 have been welcomed for giving weight to social factors in depression (an advance on the 2004 guidelines), but criticised for being too vague as to when and how clinicians should address these concerns³⁷. In the updated 2018 guidelines (draft consultation) more guidance is available with NICE recommending 'befriending' services provided by volunteers or rehabilitation programmes aimed at

reintegrating depressed patients into social activities³⁸. Social interventions aimed at dPD must take special considerations relating to PD into account, for example, fear of falling causes PwP to avoid taking part in activities (and is associated with worse depression and anxiety)³⁹.

Evidently, social factors contribute to dPD and depression in general, and there remains an unmet need for effective social interventions. The urgency for this is emphasized by a NICE recommendation for research studying the effectiveness of peer support and group-based exercise therapy for depression with a chronic physical health condition⁴⁰.

Intimacy

Being generally elderly, sexual intimacy is often thought of by PwP as implausible given their age and motor dysfunction⁴¹, despite desire remaining. This means that sexual intimacy may be overlooked, or never mentioned to physicians. Ben mentioned that he was saddened by lack of sexual intimacy in our first conversation, even ruefully encouraging me to 'enjoy it while you can'. When asked why he hadn't spoken to his GP about this, he responded that 'they can't help'. Though there might not be a cure for his impotence, broaching this topic might have led to exploration of underlying concerns. In particular a loss of a sense of masculinity is a documented concern for PwP⁴¹. Furthermore solutions to re-establish sexual intimacy, or encouragement to emphasize other forms of intimacy, might have been suggested, as lack of recreational intimacy is associated with depression amongst PwP⁴². Belief that they are too old, or embarrassment might prevent patients from raising concerns over sexual intimacy. Therefore, physicians should take an active role in asking about these issues, especially given evidence from a longitudinal study associating sexual activity with lower depression scores in PwP⁴³.

Psychological factors

Coping styles

Coping refers to the strategies we employ in response to stressors. The term coping styles is used to refer to a broad group of similar coping strategies⁴⁴ (summarised in Table 1). It is widely accepted that avoidant styles of coping are maladaptive. Indeed, a systematic review linked avoidant coping styles to worse psychological outcomes in patients with chronic disease and disability⁴⁵.

Table 1: A summary of coping styles and individual coping strategies⁴⁴

Active-cognitive style	
Staying positive	Acceptance
Planning ahead	Preparing for the worst
Active-behavioural style	
Seeking professional help	Seek help from family and friends
Getting information about the disease	Exercise

Avoidant style	
Avoid discussions about disease	Avoid information about disease
Trivialisation or wishful thinking	Not vocalising feelings

Avoidant coping is likely to increase risk of dPD^{31,42}. Evans and Norman found that avoidant coping styles were associated with greater psychological distress in a study of 67 PwP⁴⁶. Furthermore, Ehmann et al. showed that use of avoidant coping was associated with worse depressive symptoms in PwP⁴⁷. It should be noted that a bidirectional influence between dPD and avoidant coping is likely to exist, as depression, characterised by apathy, lack of motivation etc. may manifest as attitudes which can be described as avoidant. In the other direction, avoidant coping styles may exacerbate depressive symptoms by delaying requests for help/therapy as well as simply being ineffective in the face of worsening symptoms that cannot be ignored.

Ben has adopted an avoidant coping style. He mentions that he doesn't really understand what PD is and moreover does not want to know. He also relies heavily on his wife to take in information as 'she's the one who takes any interest in it'. Ben also trivialises his condition, giving an impression that he is relatively unaffected by PD when his physician reports a fairly pronounced shuffling gait and left-handed tremor. I believe Ben first adopted an avoidant coping style because it was easy to do so, as he did not perceive himself to be particularly affected by PD. Indeed, his first referral to a neurologist resulted from his wife and friends noticing his tremor and slow movement. Notice of PD symptoms by others is a reported phenomenon⁴⁸, and might reflect a sense of denial. Now that he is becoming more disabled, his avoidant coping style is certainly contributing to his depression. When asked how his attitude of 'not wanting to know' might change as his PD progresses, he responded 'I'll just have to deal with it'.

What are the determinants of coping style?

Frazier proposed the contextual and dispositional models of how coping styles may relate to disease progression⁴⁹. The contextual model is rooted in a patient's reaction to their situation, and therefore is dynamic and reflects disease progression. On the other hand, the dispositional model, being rooted on the patient's past experiences and personality, is independent of disease progression and remains stable. Ben illustrates that these two influences on coping style are not mutually exclusive. Contextually, his adoption of a coping strategy of not wanting to know reflects early stages of PD progression with perceived mild symptoms. Dispositionally, his 'stubbornness' (described by his wife) also influences his assertion that he's 'not cut out to understand' medical information. A recent study reporting coping style change as PD symptoms become more severe supports the contextual model⁵⁰ and thus suggests that Ben's adoption of an avoidant coping style at early disease progression may be common amongst PwP. In line with this, Liao et al. broke down patient perceptions of disease progression into four stages, from ignorance of symptoms (stage 1) to full dependence on others (stage 4)⁴⁸. According to the contextual model of coping style, stage 1 might predispose some PwP to adopt avoidant coping styles, which may be the most natural mechanism of coping in stage 1 but may lead to worse psychological outcomes in later stages of disease. Indeed, Liao et al. recommend providing PwP with more information in stage 1⁴⁸.

Promisingly, a randomised controlled trial of a 6 week patient education programme improved HrQoL and increased active coping styles in a study of German PwP⁵¹. This programme focussed on the psychosocial impacts of PD and developing helpful coping strategies⁵¹. NICE guidelines for management of depression in chronic disease recommend psychoeducation as an early intervention⁵². Adoption of a seminar style of providing this education (as in the German trial) could simultaneously allow PwP to meet others with PD which can have an additional positive social effect⁵¹. Early provision of education is key to avoiding establishment of avoidant coping styles which are then difficult to correct. Ben maintains; 'I'm too far down the road and I don't want to start learning things now'.

It is reasonable to expect that poor social support may predispose towards avoidant coping. Indeed, Ehmann et al. found a correlation between poorer social support and increased use of avoidant coping styles in PwP⁴⁷. Ben's social support has been significantly impacted by the illness of his wife (who is his key caregiver) and the divorce of his son and subsequent distancing from his grandchildren. As he forms a key part of their social support, Ben's avoidant coping style may be rooted in his desire to not detract attention away from his wife and son's issues. Ben becomes particularly distressed when discussing his son's divorce and its impact on his grandchildren, saying that he 'just can't handle it'. This may constitute rumination, serving as a maladaptive distraction from actively coping with PD, which itself is a form of avoidant coping⁴⁴.

The need for intervention

I would argue that due to the slow progression of disease and potential for relatively low levels of disability at diagnosis, avoidant coping styles are developed by PwP and tolerated by physicians at early stages of PD. As patient self perception of disability was found to be the major predictor of dPD in UK PwP¹², denial as a form of avoidant coping may be a natural choice until disease severity simply becomes undeniable to the patient, at which point avoidant coping becomes maladaptive.

Several authors have suggested interventions aimed at influencing coping styles as treatment for dPD^{46,53,54}. Whilst NICE guidelines for treatment of non-motor PD symptoms state that PD nurse specialists should act as a source of information to patients⁵⁵, primary care physicians may be better placed to recognise avoidant coping styles and seek interventions. This is partly because for Ben, his avoidant coping style inherently requires conceding some agency in the patient-doctor relationship; 'I prefer that they do the worrying, not me', shifting towards an interpretive model of decision making in which the doctor acts as an agent^{56,57}. For cancer patients, it has been similarly argued that it would be beneficial for doctors to take note of patient coping styles and adjust the patient-doctor relationship to prevent maladaptive ones^{58,59}.

Facilitating the patient's wish to not engage with the disease may be seen as most respectful in terms of patient autonomy. This may ultimately be true but does not preclude the need for psychoeducation for patients into the potential harms of certain forms of coping⁵¹. Evidence that motor symptoms⁵⁰ and social support⁴⁷ are determinants of coping style may suggest that maladaptive coping mediates the relationship between depression and it's biopsychosocial determinants, and at least indicate that carers should be cognizant of maladaptive coping as an indicator that upstream factors need to be addressed.

Conclusion

Ben was informed by his neurologist that PwP are more likely to feel anxious or depressed. The initial impression from this statement is that PD neuropathology predisposes PwP to mood disorders. Yet, this fails to encapsulate the myriad of biopsychosocial factors driving the high prevalence of dPD and variance amongst the PD population. Bidirectionality between depression and its determinants has been a common theme throughout this essay. Rather than view this as a confounding factor, it is necessary to recognise that this is fundamental to adopting an effective biopsychosocial model of illness⁶⁰. Integration of biopsychosocial factors best serves an understanding of dPD, for example, pain catastrophizing is hypothesized to be an attempt by patients to increase empathy and social support^{20,61}. Ben's alarming lack of engagement with PD, manifesting as an avoidant coping strategy, and his distress over recent traumatic events in his family, are two poignant reminders of the complexity of dPD. Pharmacotherapy alone is highly unlikely to be the answer, and although the importance of coping and social support are increasingly recognised as drivers of dPD, effective interventions are urgently required.

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