Describe and Evaluate the Biological Model and the Appropriate Intervention for Anxiety Disorders

School of Psychology

Bangor University

PPP2016

Describe and Evaluate the Biological Model and the Appropriate Intervention for Anxiety Disorders

Anxiety disorder (AD) is an umbrella term for a number of anxious disorders including Generalized Anxiety disorder (GAD), Panic disorder, and Obsessive-Compulsive disorder (Baldwin et al., 2014; Barton, Karner, Salih, Baldwin, & Edwards, 2014). The Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) criteria for previously mentioned ADs are in Table 1, other AD symptoms are listed in the DSM fifth addition (see American Psychiatric Association, 2013). The core symptoms of ADs are excessive worry, difficulty to control worry, and worrying significantly effecting a person's life. The international classification of disorders has a similar set of criteria for ADs (World Health Organization, 1992). The biological approach to ADs comprises of abnormal brain activity as the basis of ADs, specifically involving the amygdala (Etkin et al., 2004; Kim et al., 2011; Nutt, Ballenger, Sheehan, & Wittchen, 2002), and suggests treatment for ADs should take a pharmaceutical route (Baldwin et al., 2013; Barton et al., 2014). However, the aetiology and prognosis of ADs from a biological perspective does not lead to efficient assessment and treatment of ADs, and alternative perspectives like the biopsychosocial approach do.

The biology causing anxiety is not known (Barton et al., 2014; Nutt et al., 2002). Dysregulated levels of serotonin (Eison, 1990, as cited in Connor & Davidson, 1998), as well as abnormal activity (Barton, et al., 2014), that is, elevated metabolic rates, in the occipital, temporal, and frontal lobes (Wu et al., 1991, as cited in Connor & Davidson, 1998), have been purported as the basis for ADs. With focus on the fear and anxious component of ADs, it has been found that activation of the amygdala is greater in people with anxiety (Etkin et al., 2004; Kim et al., 2011; Nutt et al., 2002). The amygdala is responsible for emotional and fear responses (McHugh, Deacon, Rawlins, & Bannerman, 2004). Abnormalities in the brains

structure and chemistry can explain associated AD behaviours such as generalised distress, excessive worry, fearfulness, and low mood (Eley et al., 2003).

One treatment for ADs is the administration of benzodiazepines (BZs) which were a popular first stage of treatment for GAD in 1992 (Nutt et al., 2002). BZs work as gamma-aminobutyric acid (GABA) agonists on the $GABA_A$ receptor (Baldwin et al., 2013; Barton et al., 2014). As GABA is an inhibitory neurotransmitter in the brain, the high affinity of benzodiazepines with $GABA_A$ receptors means that the receptor is more likely to open the chloride channel and cause a hyperpolarisation (see Baldwin et al., 2013). This means BZs create inhibition. There are vast BZ receptors in the amygdala (McHugh et al., 2004) which can explain BZs behavioural effects such as reducing fear. Benzodiazepines can also alleviate the experience of anxiety through inhibition, by reducing muscle tension, aiding sleep, normalising hypervigilance, and reducing acute symptoms of anxiety on a two- to four-week course (Barton et al., 2014; Starcevic, 2014). However, there are negative side-effects of BZs as a treatment for ADs, as presented in Table 2, and withdrawal from BZs can lead to worse anxiety. Although, it has been suggested that whether or not a clinician believes BZs are addictive or harmful, depends on their exposure to BZ abuse, those with limited exposure tend to not fault BZs (Starcevic, 2014)

There are also cognitive side effects of benzodiazepines, such as anterograde amnesia, disinhibition, and delirium, especially in older adults (Clegg & Young 2011) as BZs exaggerate the normal decline of cognitive function (Griffin III, Kaye, Bueno, & Kaye, 2013 2013). Anterograde amnesia occurs even at low concentrations, meaning memories that are episodic and occur after drug absorption may not be committed to long term memory (Tan, Rudolph, & Lüscher, 2011; Uzun et al., 2010). Whilst anterograde amnesia may be beneficial during perioperative environments, that is, before surgery, this is not a normally sought after effect (Griffin III et al., 2013). Therefore, whilst BZs can help with the biological over

activity of anxiety through inhibition, and reduce the behaviours of anxiety such as generalised distress, but they have negative side effects which could decrease their desirability.

The National Institute for Health and Care Excellence (NICE; as cited in Barton et al., 2014) recommends pharmacological treatment such as selective serotonin reuptake inhibitors (SSRIs) and selective noradrenaline and serotonin reuptake inhibitors (SNRIs) as these have less negative affects compared to BZs (Barton et al., 2014). They aim to regulate serotonin levels, by limiting serotonin and/or noradrenaline reuptake. However, it has been suggested that SSRIs and BZs have the same withdrawal symptoms and some studies which suggest that SSRIs somehow combat the withdrawal are not supported (Nielsen, Hansen, & Gøtzsche, 2012). The shift from BZs to SSRIs also came from a period of little research into the comparative benefit of either drug, and was argued a premature move (Berney et al., 2007). The move to SSRIs may not have been to better treat patients, but because they are more cost effective drug (Heuzenroeder et al., 2004). Therefore, whilst SSRIs and SNRIs were supposed to be a better treatment for anxiety, they may not provide any more benefit than BZs. However, BZs and SSRIs target different brain activity, and combinations of both are not used due to side effects, it is possible that a patient will not receive full treatment due to only targeting one type of brain dysfunction (i.e., serotonin or amygdala inhibition).

Furthermore, the biological approach does not lend to an effective assessment process due biological individual differences. Two people that are anxious may not have the same brain activity, this could be due to natural brain variations, or general differences in their disorder diagnosis (Heller, Nitschke, Etienne, & Miller, 1997). There are also variations within groups of participants, with some having abnormal brain activity and some having normal activity, yet the same diagnosis (Owens & Nemeroff, 1994). Also, two disorders may have similar brain activity, for instance low serotonin levels are implicated in both anxiety

and depression (Connor & Davidson, 1998; Owens & Nemeroff, 1994). The variation means that assessment is difficult as it cannot rely on brain activity in one region, a specific type of activity, or higher or lower chemical levels, for a specific diagnosis. Treatments based on this screening that target specific brain activity might not be effective because of the variation. Therefore, diagnosis from this approach can be hard, as it is not just brain activity that needs to be considered but other symptoms that differentiate disorders. There is also debate that if biological screening were to come into place, it could lead to stigmatisation and discrimination of different brain activity (Patch, Roderick, & Rosenberg, 2005).

The flaw with the biological approach is the diagnosis of a person based on just biological factors, when a person could be influenced by many factors (Engel, 1980). A better approach for assessment and treatment of ADs is the Biopsychosocial model (BPSM) which takes into account biology, behaviour, and psychology. The BPSM encompasses a hierarchy of systems which are all joint by their connection to the individual; to look at one is to look at another (Engel, 1980). The person is at the centre, with considerations for the interaction between person and doctor they are talking to, the patient's nervous system, organ system, cell and molecular level, as well as family history and wider community (Engel, 1980; Fava & Sonino, 2007). This model includes the patient's own interpretation of events, which the biological perspective does not, for instance asking someone 'are you anxious' rather than assuming from their neurochemistry. By taking into account the experience of the person, their history, their environment (i.e., stressors) as well as their biology, a more thorough diagnosis can be made. With the right diagnosis, treatments can be more effective as they tackle the specific disorder a person has that might be different from someone else with similar symptoms.

A treatment plan from the BPSM advocates a course of cognitive behavioural therapy and SSRIs, which is in line with the NICE guidelines, which recommend psychological

interventions before pharmaceutical ones, or in conjunction (NICE, 2011; NICE, 2013). Interventions with psychological and pharmaceutical treatments are more effective and more long term than just drug interventions or just therapy (Bandelow, Seidler-Brandler, Becker, Wedekind, & Rüther, 2007). Therefore, the BPSM provides a more thorough assessment process, taking into account individual differences and differentiates between disorders.

In conclusion, the biological approach has a focus on brain activity which leads to associated behaviours of anxiety. However, this approach fails to acknowledge the variation of brain activity associated with ADs and may not provide the best perspective for viewing the whole of a person's disorder, and differences between disorders. The BPSM takes into account factors beyond biology that could impact ADs and provides for better treatment ideas, which has been more effective than pharmaceuticals alone based on evidence. Therefore, the biological approach fails to account of potentially important factors contributing to ADs, does not contribute an effective screening process, and provides treatments which focus mainly on one system in the brain and not all.

Word count: 1498

References

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM-5. Washington, D.C: American Psychiatric Association. Retrieved from https://ebookcentral.proquest.com/lib/bangor/reader.action?docID=1811753

Baldwin, D. S., Aitchison, K., Bateson, A., Curran, H. V., Davies, S., Leonard, B., ... & Wilson, S. (2013). Benzodiazepines: risks and benefits. A reconsideration. *Journal of Psychopharmacology*, *27*(11), 967-971. doi: 10.1177/0269881113503509

Baldwin, D. S., Anderson, I. M., Nutt, D. J., Allgulander, C., Bandelow, B., den Boer, J. A., ... & Malizia, A. (2014). Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *Journal of Psychopharmacology*, *28*(5), 403-439. doi: 10.1177/0269881114525674

Bandelow, B., Seidler-Brandler, U., Becker, A., Wedekind, D., & Rüther, E. (2007). Meta-analysis of randomized controlled comparisons of psychopharmacological and psychological treatments for anxiety disorders. *The World Journal of Biological Psychiatry*, *8*(3), 175-187. doi: 10.1080/15622970601110273

Barton, S., Karner, C., Salih, F., Baldwin, D. S., & Edwards, S. J. (2014). Clinical effectiveness of interventions for treatment-resistant anxiety in older people: a systematic review. *Health Technology Assessment*, *18*(50), 1-60. doi: 10.3310/hta18500

Berney, P., Halperin, D., Tango, R., Daeniker-Dayer, I., & Schulz, P. (2007). A major change of prescribing pattern in absence of adequate evidence: benzodiazepines versus newer antidepressants in anxiety disorders [Abtract]. *Psychopharmacology bulletin*, *41*(3), 39-47. Abstract retrieved from Abstratcs in PubMed. (PMID: 18779775).

Clegg, A., & Young, J. B. (2011). Which medications to avoid in people at risk of delirium: a systematic review. *Age and ageing*, *40*(1), 23-29. doi: 10.1093/ageing/afq140

Connor, K. M., & Davidson, J. R. (1998). Generalized anxiety disorder: neurobiological and pharmacotherapeutic perspectives. *Biological psychiatry*, *44*(12), 1286-1294. doi: 10.1016/S0006-3223(98)00285-6

Eley, T. C., Bolton, D., O'connor, T. G., Perrin, S., Smith, P., & Plomin, R. (2003). A twin study of anxiety-related behaviours in pre-school children. *Journal of Child Psychology and Psychiatry*, *44*(7), 945-960. doi: 10.1111/1469-7610.00179

Engel, G. L. (1980). The clinical application of the biopsychosocial model. *American J ournal of Psychiatry*, *137*(5), 535-544. doi: 10.1176/ajp.137.5.535

Etkin, A., Klemenhagen, K. C., Dudman, J. T., Rogan, M. T., Hen, R., Kandel, E. R., & Hirsch, J. (2004). Individual differences in trait anxiety predict the response of the basolateral amygdala to unconsciously processed fearful faces. *Neuron*, *44*(6), 1043-1055. doi: 10.1016/j.neuron.2004.12.006

Fava, G. A., & Sonino, N. (2007). The biopsychosocial model thirty years later. *Psychotherapy and psychosomatics*, *77*(1), 1-2. doi: 10.1159/000110052

Griffin III, C. E., Kaye, A. M., Bueno, F. R., & Kaye, A. D. (2013). Benzodiazepine pharmacology and central nervous system–mediated effects. *The Ochsner Journal*, *13*(2), 214-223. doi: 10.1043/1524-5012-13.2.214

Heller, W., Nitschke, J. B., Etienne, M. A., & Miller, G. A. (1997). Patterns of regional brain activity differentiate types of anxiety. *Journal of Abnormal Psychology*, *106*(3), 376. doi: 10.1037/0021-843X.106.3.376

Heuzenroeder, L., Donnelly, M., Haby, M. M., Mihalopoulos, C., Rossell, R., Carter, R., ... & Vos, T. (2004). Cost-effectiveness of psychological and pharmacological interventions for generalized anxiety disorder and panic disorder. *Australian and New*

Zealand journal of psychiatry, *38*(8), 602-612. doi: 10.1111/j.1440-1614.2004.01423.x

Kim, M. J., Loucks, R. A., Palmer, A. L., Brown, A. C., Solomon, K. M., Marchante, A. N., & Whalen, P. J. (2011). The structural and functional connectivity of the amygdala: from normal emotion to pathological anxiety. *Behavioural brain research*, *223*(2), 403-410. doi: :10.1016/j.bbr.2011.04.025

McHugh, S. B., Deacon, R. M. J., Rawlins, J. N. P., & Bannerman, D. M. (2004). Amygdala and ventral hippocampus contribute differentially to mechanisms of fear and anxiety. *Behavioral neuroscience*, *118*(1), 63. doi: 10.1037/0735-7044.118.1.63

NICE. (2011). *Common mental health problems: identification and pathways to care*. Retrieved from https://www.nice.org.uk/guidance/CG123/chapter/1-Guidance#stepped-care

NICE. (2013). *Social anxiety disorder: recognition, assessment, and treatment*. Retrieved from https://www.nice.org.uk/guidance/cg159

Nielsen, M., Hansen, E. H., & Gøtzsche, P. C. (2012). What is the difference between dependence and withdrawal reactions? A comparison of benzodiazepines and selective serotonin re-uptake inhibitors. *Addiction*, *107*(5), 900-908. doi: 10.1111/j.1360-0443.2011.03686.x/epdf

Nutt, D. J., Ballenger, J. C., Sheehan, D., & Wittchen, H. U. (2002). Generalized anxiety disorder: comorbidity, comparative biology and treatment. *International Journal of Neuropsychopharmacology*, *5*(4), 315-325. doi: 10.1017/S1461145702003048

Owens, M. J., & Nemeroff, C. B. (1994). Role of serotonin in the pathophysiology of depression: focus on the serotonin transporter. *Clinical chemistry*, *40*(2), 288-295. Retrieved from http://clinchem.aaccjnls.org/content/40/2/288/tab-article-info

Patch, C., Roderick, P., & Rosenberg, W. (2005). Comparison of genotypic and phenotypic strategies for population screening in hemochromatosis: assessment of anxiety, depression, and perception of health. *Genetics in Medicine*, *7*(8), 550-556. doi: 10.1097/01.GIM.0000182466.87113.ce

Starcevic, V. (2014). The reappraisal of benzodiazepines in the treatment of anxiety and related disorders. *Expert review of neurotherapeutics*, 14(11), 1275-1286. doi: 10.1586/14737175.2014.963057

Tan, K. R., Rudolph, U., & Lüscher, C. (2011). Hooked on benzodiazepines: GABA A receptor subtypes and addiction. *Trends in neurosciences*, *34*(4), 188-197. doi: 10.1016/j.tins.2011.01.004

Uzun, S., Kozumplik, O., Jakovljević, M., & Sedić, B. (2010). Side effects of treatment with benzodiazepines. *Psychiatria Danubina*, *22*(1), 90-93. doi:

Wafford, K. A. (2005). GABA A receptor subtypes: any clues to the mechanism of benzodiazepine dependence? *Current opinion in pharmacology*, *5*(1), 47-52. doi: 10.1016/j.coph.2004.08.006

World Health Organization. (1992). *The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization. Retrieved from http://apps.who.int/iris/bitstream/10665/37958/8/9241544228_eng.pz

Appendix A

Table 1

The diagnostic criteria for anxiety disorders summarised from the DSM fourth edition

Disorder	Criteria for diagnosis
Generalized Anxiety Disorder (GAD)	Excessive worry above a situation, worry across many situations and days for a sixth month period Difficulty to control worry At least three symptoms from this list: restlessness or feeling keyed up or on edge; easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension; sleep disturbance AD is not caused by substance abuse
Obsessive-Compulsive disorder (OCD)	Obsessions are defined as recurrent thoughts that could cause anxiety, that are not just worries about life, the person attempts to ignore/neutralise them, and the person recognises that they are obsessional Compulsions are repetitive behaviours that a person feels driven to perform in response to an obsession, and they are aimed to reduce stress/anxiety, however these acts are not done in a realistic way that would deal effectively with the obsession At some point the person has realised the obsessions and compulsions are excessive or unreasonable The obsessions and compulsions caused distress and significantly interfere with the person's normal routine/functioning OCD is not the result or partnered with another disorder The OCD is not caused by a substance
Panic disorder	Recurrent unexpected panic attacks, at least one a month, with persistent concern about additional attacks, worry about consequences of attacks, and significant change in behaviour related to attacks Absence or presence of agoraphobia Panic attacks are not caused by substances (e.g., drugs) Panics attacks are not better explained by another disorder such as social phobia, OCD, PTSD etc

Note. Information taken from "Diagnostic criteria for anxiety disorders set out in DSM-IV and ICD-10 classification systems" by Barton, S., Karner, C., Salih, F., Baldwin, D. S., & Edwards, S. J. (2014). Clinical effectiveness of interventions for treatment-resistant anxiety in older people: a systematic review. *Health Technology Assessment*, *18*(50), 1-60.

Appendix B

Table 2

Side-effects of Benzodiazepines

Drug	Side-effects
Benzodiazepines	Tolerance to drug (Baldwin et al., 2013; Wafford, 2005)
	Worse anxiety if course is discontinued (Connor & Davidson, 1998)
	Depersonalisation (Baldwin et al., 2013)
	Sweating, muscular pain, fatigue, palpitations, numbness, and irritability (Nielsen, Hansen, and Gøtzsche, 2012)
	Disinhibition (Griffin III et al., 2013)
	Delirium (Clegg & Young, 2011)
	Anterograde amnesia (Tan, Rudolph, & Lüscher, 2011; Uzun et al., 2010)