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Fear and anxiety: Lessons learned from the Dunedin longitudinal study

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ABSTRACT

Four related lines of research on anxiety were reviewed from the 'Dunedin Study', an investigation of a representative longitudinal birth cohort of 50-years duration, with 94% retention at the last follow-up. Findings include: (i) Childhood fears deemed evolutionarily-relevant may have different pathways and/or mechanisms underlying their emergence when compared to evolutionarilyneutral fears. (ii) Sequential comorbidity both inside and external to the family of disorders is the rule not the exception, highlighting the importance of developmental history. (iii) The developmental relationship between GAD and MDE is more symmetric that previously assumed, with equal numbers of persons having GAD preceding MDE and MDE preceding GAD. (iv) PTSD in adulthood is influenced by a broad range of childhood risk factors, sequential comorbidity is near universal, and both high-stress life events and mental-disorder history influence the development of PTSD. The implications for epidemiology, nosology, the importance of developmental history, and prevention/treatment options are considered.

1. Introduction

Anxiety is a normal (almost ubiquitous) human emotion, but for some it can become an aversive, unwanted experience, either because it is out of proportion to the threat present, or because it persists long after the 'danger' has passed, or both.

Here we review findings about fear and anxiety disorders from a developmental perspective, using the multi-disciplinary Dunedin Study, a 50-year-longitudinal investigation of a birth cohort from the general population (born between April 1, 1972 and March 31, 1973). Since birth the 1000 Study members have been assessed repeatedly at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38 and most recently at age 45 years (2017–2019) with over 94% of the living participants still taking part.

2. Child fears

A target paper from the Dunedin Study published in a Special Issue of Behaviour Research and Therapy in 2002 set out the arguments for a 'non-associative' model of fear acquisition (Poulton and Menzies, 2002). According to this theory, the learning processes typically associated with a fear response (e.g., US-UCS pairing) were less likely to occur in the acquisition of evolutionarily-relevant fears (e.g., heights, Poulton et al., 1998), whereas such learning processes would be expected to be plentiful – either direct or indirect (modelling or information transmission) - in the acquisition of evolutionarily-irrelevant fears such as dental fear (Poulton et al., 1997, 2001). These findings were controversial, despite evidence in support of the basic idea, including for different learning processes implicated in non-associative fear acquisition, for example, fear dishabituation which describes the return of fear in the context of high levels of non-specific stress (Poulton et al., 2000), and failures in exposure to the fear stimulus, for example heights (Poulton et al., 2001). In particular, the term 'non-associative' learning appeared to cause confusion, implying as it did an absence of learning processes per se. In retrospect we should have emphasised the *different* learning processes.

For example, in a Dunedin Study test of height-fear acquisition, putative conditioning events measured prospectively up to the age of nine and the presence of height fear at ages 11 and 18 were examined. No positive relation was found between having had a history of falls resulting in injury (e.g., fracture, dislocation, intracranial injury or laceration) before age nine and fear of heights at 11 or 18. Interestingly falls resulting in injury between ages 5 and 9 occurred more frequently in those without a fear of heights at 18 ($P < 0.01$), this finding was in the opposite direction to that predicted by conditioning theory, but supportive of so-called non-associative theories of fear acquisition.

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In another study aimed to test Rachman's three associative pathways model (Rachman, 1977), the relation between separation experiences and the development of separation anxiety was examined at age 3, 11 and 18 in the same cohort of individuals. We found no relation between experiences of separation at age 3 and the subsequent measures of separation disorder. Vicarious learning (or modelling) in middle childhood was related to separation anxiety at age 11, accounting for 1.8% of the variance in symptoms, but was no longer significant in adjusted models. Lastly, separation experiences (hospitalisations) were inversely associated with separation anxiety at age 18 (Poulton et al., 2001). That is, more overnight stays in hospital during childhood were associated with less separation anxiety in late adolescence. Thus, for some simple fears at least, it is plausible that processes other than those invoked in traditional learning theory are sufficient to explain the development of clinically significant symptoms.

3. Adult anxiety disorders

Turning our attention to the anxiety disorders in adulthood, once again there appears to be a dichotomy of views. Indeed, it may not be an exaggeration to say that at the diagnostic level psychiatry seems torn between two realities. On the one hand, there are those who continue to hold to the view that a 'one point in time' diagnosis captures meaningful information about likely prognosis and response to treatment. On the other hand, a growing body of research shows that changing diagnosis, across time and even between diagnostic families, is the rule rather than the exception.

This fundamental insight, made possible by acknowledging developmental history, explains why the natural history of disorder varies so dramatically over time (Kim-Cohen et al., 2003; Caspi et al., 2014, 2020). In particular, sequential comorbidity appears to occur naturally and, with sufficient time, pervasively. It characterises all disorders, including the adult anxiety disorders, which for this review includes Generalised Anxiety Disorder, Social Anxiety Disorder, Panic disorder with and without Agoraphobia, Simple Phobia and Post-Traumatic Stress Disorder (PTSD). Obsessive-Compulsive Disorder has recently been re-categorised in the DSM-V and is empirically more aligned with the Thought Disorder family of disorders (e.g. Caspi et al., 2014).

Indeed, conceptualising disorder as being on a continuum rather than dichotomous as enshrined in the DSM system inevitably recognises the developmental history of disorders. Currently the best way to conceptualise disorder, at a more granular level, is to think in terms of internalising, externalising and thought disorders, and to think also of a single vulnerability (i.e., the p-factor) at the highest level (Caspi et al., 2014, also see Kotov et al., 2022). This brief review is influenced by this framework, albeit while mainly presenting data which is based on dichotomous diagnoses.

The anxiety disorders are the most common of all mental disorders. They are also costly, both in terms of human suffering and economics (Rice and Miller, 1998). According to the National Comorbidity Study Replication they onset early in life (median age of onset for any retrospectively recalled anxiety disorder is 11 years) (Kessler et al., 2005) but with prospective designs the age of onset appears even younger, and this is true in the Dunedin Study. Anxiety disorders can be split into homogenous groups or may be lumped into a single phenotype, with some evidence favouring a 2-factor solution whereby generalized anxiety disorder pairs with depression, as distinguished from other anxiety disorders (e.g., Watson et al., 2022).

Anxiety disorders also share a risk factor profile in common, with the exception of specific phobias (see earlier discussion about the acquisition of specific fears). Lastly, treatment research points to similar effects with, for example, SSRIs being used effectively for panic disorder, generalized anxiety disorder, social anxiety disorder, and post-traumatic stress disorder, but interestingly (again) not for specific phobia (Craske et al., 2017). The increasing efficacy and popularity within psychiatry of transdiagnostic therapeutic approaches points towards similar transdiagnostic effects for Cognitive Behavioural Treatments.

According to Gregory et al. (2007), virtually all those meeting criteria for a 12- month anxiety disorder at age 32 had met criteria for a psychiatric disorder previously (88–100%.). When continuity of anxiety disorder was considered specifically at age 32, more than 75% of the Dunedin cohort had met criteria for an anxiety disorder previously (range for specific diagnoses: 78–96%), with more than one third before age 15. Examples of strict homotypic continuity can be seen as well as loosely defined homotypic continuity (at the internalising spectrum level), with individuals who had post-traumatic stress disorder also meeting diagnostic criteria for conduct and oppositional defiant disorder. Of note, adult specific phobia had a developmental history of juvenile phobias only, unlike most disorders, which had a relationship with any of childhood overanxious disorder, specific phobia and separation anxiety.

4. Generalized anxiety disorder versus major depressive episode

Historically the comorbidity between major depressive episode and generalized anxiety disorder has been assumed to reflect the temporal primacy of generalized anxiety disorder antedating major depressive disorder. That is, generalized anxiety usually precedes depression and eventually develops into depression. However, when Moffitt et al. (2007a) looked at the relationship they found it was far more equal than expected. Among Dunedin study participants presenting with depression and/or GAD by age 32, depression onset first in one third, anxiety onset first in one third, and the reminder showed concurrent onset.

A parallel study examined childhood risk factors for generalized anxiety disorder and depression and noted some important differences between the two groups (Moffitt et al., 2007b). The childhood risk factors included measures of family history, adverse family environment, childhood behaviour, adolescent self-esteem and personality traits. Findings showed that comorbid generalized anxiety disorder and depression were characterised by highly elevated risk factors broadly across all domains, whereas pure generalized anxiety disorder had elevated risk on only adverse family environment (low SES, somewhat more maltreatment) and childhood behaviour (internalising problems, conduct problems, and comparatively more inhibited temperament). In contrast, pure major depressive episode had risk factors not shared by pure generalized anxiety disorder, and these were in the domains of family history (of depression) and personality (low positive emotionality), suggesting partly different etiological pathways between the two disorders.

The take home message from the Dunedin Study and other studies is that when comorbid disorders are present, the age of onset tends to be younger, disorder has more persistent duration, and the severity and risk factor profile is worse (e.g. Caspi et al., 2020). This also augurs a more treatment-resistant version of the disorders.

5. Post-traumatic stress disorder (PTSD)

PTSD is unique among adult mental disorders because exposure to a traumatic event(s) is required to meet criteria for a clinical diagnosis.

A study from the Dunedin cohort examined the links between early-life risk factors and the development of PTSD at two time points in adulthood (Koenen et al., 2007). Childhood risk factors included neurodevelopmental, temperamental, behavioural and family environmental characteristics before age 11. These risk factors differ from those reported in the previous section. Specifically, two sets of risk factors were identified; one which increased risk for trauma exposure and the onset of PTSD at age 26. To wit maternal distress and loss of a parent increased both the risk of trauma exposure and the risk of PTSD. The second set of risk factors predicted risk for PTSD only, and included low IQ and chronic environmental adversity. Further, low IQ at age 5, antisocial behaviour, and poverty before 11 predicted PTSD that occurred between age 26 and 32, suggesting that developmental

capacities and conditions of early childhood may increase both risk of trauma exposure and of PTSD. Rather than being solely a proximal response to trauma, the roots of PTSD involve predisposing developmental origins.

A 2008 Dunedin report examined the mental health histories of PTSD sufferers. It was found that 100% of those diagnosed with past year PTSD and 93.5% of those with a lifetime PTSD diagnosis by 26 had met criteria for another disorder between at 11 and age 21. Among those new cases of PTSD arising between 26 and 32, 96% had a prior mental disorder, with 77% having been diagnosed by 15, suggesting that PTSD in adulthood rarely, if ever, develops in anything but the context of other disorders (Koenen et al., 2008).

Finally, a third study of the development of PTSD (Breslau et al., 2014) compared (i) the mental health histories of those who were likely to have adult PSTD and (ii) the experience of childhood maltreatment. Both severe maltreatment and prior history of mental disorders were found to independently predict adult PTSD. Note, the experience of mild trauma during childhood was not found to increase the risk of PTSD by the adult years, providing little evidence for the hypothesis of stress-sensitisation from moderate trauma.

6. Conclusions

Drawing on 25 + years of developmental research from the Dunedin Study about how fear, phobias and anxiety disorders emerge, we make the following conclusions. All have implications for nosology, etiology and/or prevention.

1. Some simple fears and anxiety symptoms (i.e., those that are evolutionary-relevant) may occur due to failures in learning, for example, failure to 'unlearn' an already present fear, or failure to experience fear-stimuli exposure, for example, when a child has not been exposed to heights (e.g., by climbing trees); points interestingly first made by Rachman (1978). This does not argue for a major change in theory, rather it adds more nuance to arguments about what about anxiety is 'innate' and what is 'learned'.
2. The main findings show that the anxiety disorders favour the lumper over the splitter. That is, a general approach to the classification of the anxiety disorders may be warranted. Most Dunedin cohort members with anxiety disorders had histories of prior disorders, and these tended to group around the internalising spectrum, but not exclusively. Some of specific findings, for example, that specific phobias in adulthood were only associated with prior childhood phobias, but not other disorders in the juvenile years suggest that these disorders may require different classification. In general, the findings fit well with a hierarchical approach to classification.
3. The natural history of adult anxiety disorders suggests that research aimed at understanding the etiology of fear or anxiety disorders should begin very early in life and take advantage of newer approaches to the treatment of anxiety in young children.
4. Consistent with the last point, our findings suggest that opportunities for prevention also exist early in life, an oft-repeated plea from life-course researchers for the anxiety disorders, as well as other disorders (e.g., depression, eating, and substance use disorders).
5. Given the notable longitudinal overlap between different types of anxiety disorders, focussing on the development of transdiagnostic therapeutic approaches seems warranted, particularly for 'talking therapies' like Cognitive Behavioral Therapy (e.g. Barlow et al., 2020).
6. "Schooling up" practitioners and teachers having early contact with young children so they know important age-appropriate, generic support for the anxious child seems necessary. This goal here is to pre-empt or prevent the onset of troubling anxiety in the first instance, by targeting for example, poor emotional regulation. These approaches can apply a 'teach the teacher' approach and are therefore very scalable.
7. For the practicing clinician, conceptualising problems from a developmental perspective may have advantages because it will (i) explain the focus of treatment on longstanding dysfunctional beliefs and behaviours, and (ii) improve rapport between the client and clinician because they have a shared understanding of the problem.

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