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Psychopathology and Neurocognition in the Era of the *p*-Factor: The Current Landscape and the Road Forward

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Abstract: Neurocognitive abilities have frequently been claimed to be involved in the aetiology of psychopathology. Neurocognitive deficits have been reported across many disorders, and theoretical perspectives associate these deficits to the onset and maintenance of the symptomology. Recently, the heterogeneity of symptoms, and comorbidity of disorders, have motivated the development of structural models of psychopathology. Structural models indicate that factors such as internalising, externalising, thought disorder and the *p*-factor account for a wide variety of symptomology. It is unclear how neurocognitive abilities are best examined within these structures to advance our understanding of psychopathology. In this paper, we use Caspi et al.'s seminal writings as a framework to describe how neurocognitive abilities have been previously associated with categorical disorders and recently associated, and claimed to drive, the factors of psychopathology. We discuss the implications of the *p*-factor as a substantive construct or statistical artefact, and how this impacts the exploration of neurocognitive abilities and psychopathology. Further, we provide the case for alternative structural approaches, describe an innovative hypothesis of neurocognitive functioning, the *multidimensional hypothesis*, and explain how this may further our understanding of the heterogeneity of neurocognitive performance and psychopathology at the individual level. Finally, we provide a road forward for the future examination of neurocognitive abilities in psychopathology.

Keywords: neurocognition; executive function; psychopathology; multidimensional; *p*-factor; bifactor; correlated factors; s-1 bifactor; disorders

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1. Introduction

A consensus exists within the study of typical human development that variability in neurocognitive abilities accounts for a large proportion of individual differences in domains such as problem solving, reasoning, thinking and planning. Furthermore, deficits in neurocognitive processes have been repeatedly implicated in studies of psychopathology [1]. For example, deficits in the executive function (EF) processes of shifting, updating and inhibition have each been separately argued to explain symptoms of schizophrenia (e.g., [2–4]), depression [5–7] and substance use disorder [8–10]. However, the literature shows little agreement as to which neurocognitive processes are of primary importance in any given disorder. One reason for this is that, within the context of clinical diagnoses, individuals diagnosed with the same psychopathological disorder can exhibit markedly different symptoms. Another reason is that many individuals diagnosed with a specific psychopathological disorder are also found to meet the criteria for other disorders [11]; thus, making the *pure* study of any given disorder more challenging.

Issues to do with the heterogeneity of symptoms and the comorbidity of disorders have motivated the development of a number of structural models of psychopathology aimed at accounting for covariation amongst psychopathology and providing a dimensional framework that can be used for the description and understanding of psychopathology [12–14]. Whilst in some instances transdiagnostic approaches have been hailed as achieving a degree of success (e.g., [15–17]), an explanation of the *mechanisms* of dysfunction remains limited.

In this paper, we discuss some of the main issues that have prevailed within the classification and study of psychopathology, and discuss the development of dimensional structural models of psychopathology. We use Caspi et al.'s [13] seminal work as a basis of this paper due to its popularity and how recent literature has used their findings to further develop the understanding of structural models of psychopathology, thereby facilitating discussion of the development of this literature. We describe the rise of the *p*-factor and components claimed to be integral to the factor's existence, as well as the debate surrounding the nature of the *p*-factor as a substantive or artefactual construct. We briefly review key neurocognitive accounts relating to the basis of psychopathology and how dimensional models may facilitate the exploration of the association between psychopathology and neurocognitive abilities and describe the *multidimensional hypothesis* [18]. This hypothesis is based on the idea that psychopathologies are rarely the consequence of deficits to single neurocognitive mechanisms. Rather that cognitive dysfunctions are more often the outcome of the dynamics of a system comprised of uneven profiles in abilities. We conclude by providing a road forward for the better understanding of the relation between neurocognitive mechanisms and psychopathology.

2. Classifying Psychopathology

Griesinger (1817–1868) argued for psychiatric symptoms (or "madness") being the result of a singular disease, and referred to this as the "unitary psychosis" [19]. Emil Kraepelin (1856–1926) later devised the Kraepelinian Dichotomy, the characterisation of mental disorder into dementia praecox (to be later reconceived as schizophrenia) and manic-depressive psychosis (to be later reconceived as bipolar disorder). This dichotomy led to the development of modern diagnostic manuals [19]. In the current day, psychopathology is generally defined and determined through a traditional nosological approach, classifying pathology into single, discrete categories [20]. The Diagnostic and Statistical Manual (DSM) and the International Classification of Diseases (ICD) have become standard tools used to guide the diagnosis of psychopathology [21]. However, the reliance on these tools have raised particular issues regarding *comorbidity* and *diagnostic stability*. For example, Newman et al.'s [11] work showed that of individuals who meet the diagnostic criteria for one DSM-3 defined disorder, approximately half will meet the criteria for a second, and approximately half of those will meet the criteria of a third disorder, and so on. These issues of comorbidity have also been seen in subsequent issues of the DSM (see [12]). The poor stability of disorder diagnosis is a further issue for the nosological approach. For example, a high proportion of anxiety disorders transition to a different anxiety disorder over a six-year period [22]. Aetiological similarities between disorders also suggest that disorders are not so distinct. For example, schizophrenia and bipolar affective disorder share aetiological markers across genetic, environmental, neurological and cognitive domains [23–26]. Ultimately, the high level of comorbidity between disorders, in addition to a plethora of biological, cognitive and environmental evidence, suggests that disorders are not as distinct as previously assumed [20]. On a practical level, this has many implications. For example, high levels of comorbidity and low levels of diagnostic stability makes the study of any individual disorder difficult, as well as complicates treatment decision making (see [11]).

To combat issues of comorbidity and diagnostic stability, and to better facilitate the growing aetiological evidence suggesting low-level mechanistic commonalities, a number of structural models of psychopathology have been developed (Kotov et al. [27] integrates the available evidence of structural models of psychopathology, providing a synthesised

model. However, the size and specifications of this structure makes it difficult to test and use in its entirety.). These structural models view psychopathology as dimensional and explore hierarchical relationships among psychopathological symptoms to develop subordinate and superordinate components of psychopathology. Furthermore, it has been suggested that these dimensional models may be used to inform treatment by basing and prioritising treatment decisions on the symptom dimensions at the various levels of the models' hierarchy (see [27]). The most prominent models were developed through Caspi et al.'s [13] longitudinal research. This research saw the development and assessment of hierarchical models of psychopathology that are claimed to enhance our understanding of disorders.

3. Caspi et al.'s Structural Models of Psychopathology

Caspi et al. [13] administered a battery of biological, developmental, clinical, personality and neurocognitive measures to a representative community sample of 1000 participants across a total of 11 time points over a 35-year period (ages 3, 5, 9, 11, 13, 15, 18, 21, 26, 32 and 38). Using the Diagnostic Interview Schedule [28], clinicians counted the number of symptoms each participant reported in accordance to 11 predetermined, common, DSM defined disorders at five time points (ages 18, 21, 26, 32 and 38). Disorders and symptomology assessed included various substance use disorders (e.g., alcohol, cannabis, tobacco), conduct disorder, major depressive episode, fears and phobia symptoms, obsessive compulsive disorder, mania symptoms, and schizophrenia [13]. Caspi et al. [13] showed that the array of symptoms could be reliably fit to a correlated factors model, with factors pertaining to symptom counts of each disorder over time, and three higher-order factors called *internalising*, *externalising* and *thought disorders* (see Figure 1). Figure 1 shows the 11 disorder symptom counts over time, loading onto their specific disorder factor, representing longitudinal symptomology. Figure 1 also shows the disorder specific factors then further loading onto one of the three higher-order factors of psychopathology.

Caspi et al. [13] tested another structural model of psychopathology, called the bifactor model. The bifactor model contained, not only the disorder specific and higher-order factors, but also a single General Psychopathology factor (see Figure 2). The addition of the general factor accounted for further symptom variance among all disorders included in the model, over and above that only accounted for by the internalising, externalising and thought disorder factors. In fact, the thought disorder factor was subsumed by the introduction of the general factor and so was subsequently removed from the model [13]. The bifactor model was found to be a better fit to the data than the correlated factors model, and has subsequently become highly popular in psychiatric and psychological research.

The general psychopathology factor was named the *p*-factor, in line with its likeness to the *g*-factor, originating in the literature on intelligence. Indeed, like the *g*-factor, Caspi et al. [13] argue that, conceptually, the *p*-factor is normally distributed within the population. Caspi et al. [13] took the view that general psychopathology factor is a substantive construct that determines the presence and absence of all pathological symptoms. Crucially, the higher the *p*-factor, the greater the propensity towards psychopathology. Overall, Caspi et al. [13] found that their bifactor model successfully accounted for psychopathology in a hierarchical manner. The *p*-factor accounts for the common variance of all psychopathological symptoms, while the internalising and externalising factors account for the remaining common variance of a sub-group of similar disorders, and lastly, the disorder specific factors account for symptom variance that is unique to each disorder. Following the work of Caspi et al. [13], a range of research attempted to discover what the substantive *p*-factor is (see [29]). In other words, various theoretical explications occurred regarding the substantive meaning of *p*.

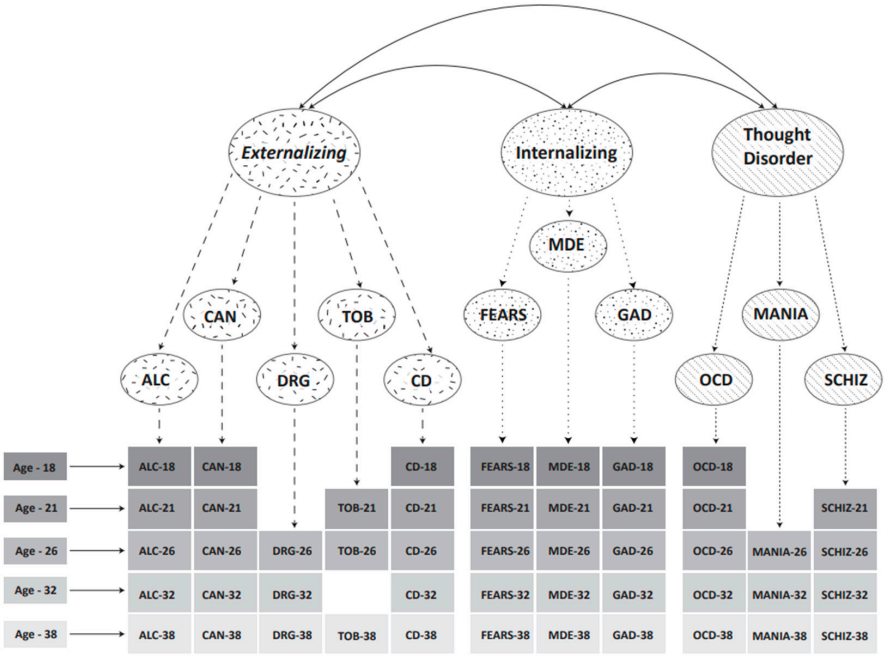

Figure 1. Adapted from Caspi et al. [13]. Ovals represent latent symptom factors; boxes represent the symptoms related to each disorder. The 11 disorders included in the model are: alcohol dependence, cannabis dependence, dependence on hard drugs, tobacco dependence, conduct disorder, major depression, generalized anxiety disorder, fears/phobias, obsessive-compulsive disorder, mania, and positive and negative schizophrenia symptoms. *Note*. ALC = Alcohol. CAN = Cannabis. DRG = Hard drugs. TOB = Tobacco. CD = Conduct disorder. MDE = Major depressive episode. GAD = General Anxiety Disorder. OCD = Obsessive Compulsive Disorder. SCHIZ = Schizophrenia.

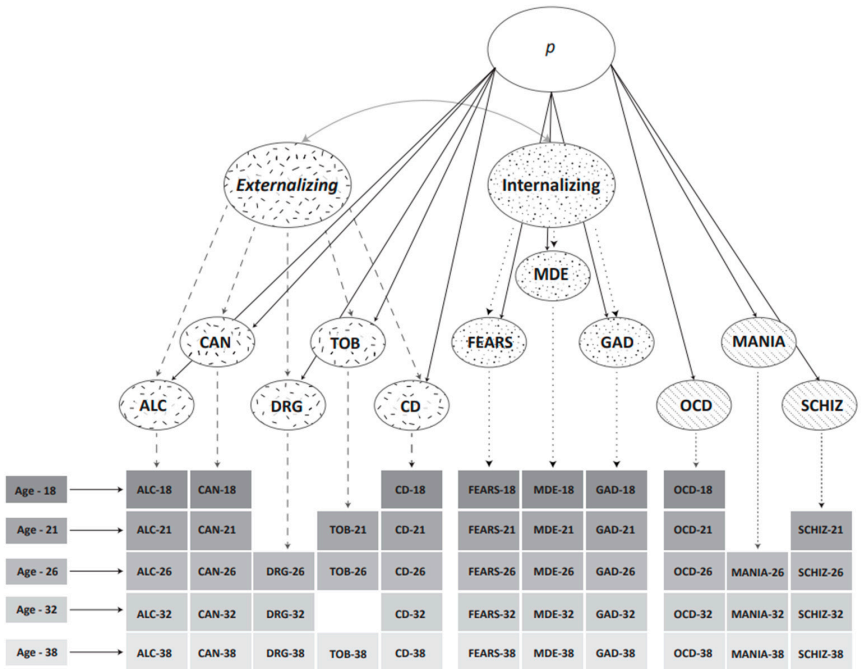

Figure 2. Adapted from Caspi et al. [13]. Ovals represent latent symptom factors; boxes represent the symptoms related to each disorder. The 11 disorders included in the model are: alcohol dependence, cannabis dependence, dependence on hard drugs, tobacco dependence, conduct disorder, major depression, generalized anxiety disorder, fears/phobias, obsessive-compulsive disorder, mania, and positive and negative schizophrenia symptoms. *Note*. ALC = Alcohol. CAN = Cannabis. DRG = Hard drugs. TOB = Tobacco. CD = Conduct disorder. MDE = Major depressive episode. GAD = General Anxiety Disorder. OCD = Obsessive Compulsive Disorder. SCHIZ = Schizophrenia.

4. What Is the *p*-Factor?

As the *p*-factor is claimed to determine an individual's overall propensity toward psychopathology [13], knowing the substrative meaning of *p* has potentially important implications for the understanding and treatment of psychopathology. A range of conflicting research has laid claim to the substantive meaning of *p*. For example, research has evidenced neuroticism as the primary driver of the *p*-factor [30], and other research has offered that *p* represents functional impairment [31], impulsive responsivity to emotion [32], or disordered thought [33]. Each of these proposals make conceptual sense. However, each of the explanations are of high-level psychological domains, underpinned by a range of other mechanisms. Therefore, other lower-level mechanisms, in particular neurocognitive abilities, have been claimed to be a primary driver of the general factor (see [34]).

Indeed, each explanation for the *p*-factor, neuroticism, functional impairment, impulsive responsivity to emotion, and disordered thought are significantly accounted for by a range of neurocognitive abilities [13,31,33,35]. Furthermore, neurocognitive abilities are also significantly associated with the internalising, externalising and thought disorder factors in Caspi et al.'s [13] correlated factors model, as well as the *p*-factor of psychopathology in the bifactor model. In fact, Caspi et al. [13] found that, from age 3 to age 38, every direct measure of neurocognitive ability was significantly associated with the *p*-factor. Furthermore, a systematic review of risk factors predictive of the statistically derived factors of psychopathology in young people found deficits in neurocognitive abilities to be a primary risk factor for higher psychopathology factor scores [36]. Ultimately, there is evidence that neurocognitive abilities are not only related to diagnosed pathologies, but even within the general population, neurocognitive abilities are related to the proposed *propensity toward psychopathology* [13]. The importance of neurocognitive abilities in the understanding of the *p*-factor, and bifactor models of psychopathology generally, has been communicated early on from Caspi et al.'s [13] longitudinal work. For example, Snyder et al. [1] proposed that the exploring associations between Caspi et al.'s [13] bifactor model and executive functioning " . . . has the potential to greatly clarify the nature of EF impairments associated with particular forms of psychopathology, and thus accelerate progress in understanding how EF impairments may contribute to both comorbidity across disorders and heterogeneity within disorders . . . " (p. 17). To set the scene for our discussion of neurocognitive abilities and structural models of psychopathology, in the following section we summarise the primary neurocognitive abilities used in clinical research, as well as each ability's association with Caspi et al.'s [13] components of psychopathology.

4.1. Neurocognitive Abilities as Important to the Factors of Psychopathology

Cognition partly consists of higher-level processes and components. These components include problem solving abilities and the control of attention, among other higher-level human abilities [37,38]. Baddeley [39] famously proposed a single component, termed the executive, which governs, organises and controls high-level abilities. Various accounts of the executive exist, raising contention as to whether the executive is a unitary component or a collection of components (e.g., [38,40,41]). However, there is broad agreement regarding the existence and importance of the executive(s) as fundamental to the control of cognition. Recently, the term executive functioning has become the norm to describe these control processes, and most work has been focused upon the three executive functioning components described by Miyake et al. [41] namely, updating, shifting and inhibition. The role of each executive function component differs. Updating is considered to be involved in the removal, addition and monitoring of the contents of working memory; shifting is involved in disengaging with the present mental set and engagement with a more relevant mental set, while inhibition is described as the process that suppresses a dominant response that is not currently useful [41]. Additionally, other singular neurocognitive components have been considered in both the theoretical and empirical domains. The most prominent of these neurocognitive components include speed of processing [42] and working memory capacity [39]. Speed of processing relates to the speed at which individuals can process

information [43], while working memory capacity is considered as the amount of information that can be held in working memory and is often conceptualised and measured in accordance with working memory updating [39,41].

Lezak et al. [37] argue that the proper functioning of these neurocognitive abilities, including executive function, are crucial to everyday behaviours, including the control of appropriate, goal-oriented and responsible behaviour. It is perhaps therefore unsurprising that abnormalities in these processes have been repeatedly indicated in a variety of psychopathologies.

4.2. Deficits in Neurocognitive Processes and Their Relation to Psychopathology

It is often suggested that deficits in neurocognitive abilities underlie pathological symptoms across Caspi et al.'s [13] factors of psychopathology. The following subsections present examples of symptoms of internalising, externalising and thought disorders that have been suggested to be underpinned by neurocognitive abnormalities.

4.2.1. Internalising

Neurocognitive deficits have been proposed to underlie a range of symptoms associated with internalising disorders. Deficits in the updating and capacity of working memory has been suggested to be central to elevated rumination in depression, due to issues in removing negative material from working memory [7]. Similarly, deficits in shifting mental set are claimed to underlie issues in shifting attention away from negative thoughts and stimuli in anxiety [43]. Inhibition has been seen to be an important aetiological mechanism in a range of internalising symptoms. For example, depression is often accompanied by a range of negative attentional and memory biases and deficits in inhibition that are proposed to underlie this issue [5,6]. Another salient symptom of depression is a general cognitive slowing [44], and this often has a great impact on the life of the person and is said to be underlain by speed of processing deficits [44].

4.2.2. Externalising

Externalising disorders, including behavioural and substance use disorders, are strongly associated with a range of neurocognitive abilities. For example, working memory deficits are said to mediate disinhibited decision making in externalising disorders [45,46]. Another example is that deficits in shifting mental set are claimed to underlie the poor consideration of behavioural outcomes in substance addiction [10]. Furthermore, the uncontrolled intake of substances has also been claimed to be associated with deficits in inhibition [9]. Speed of processing is often associated with aspects of behavioural disorders such as attention-deficit/hyperactivity disorder. For example, speed of processing issues are claimed to underlie reading fluency issues often seen in ADHD [47,48].

4.2.3. Thought Disorder

Thought disorders, such as schizophrenia and mania in bipolar disorder, have been subject to a large amount of neurocognitive research. There has been broad suggestion that deficits in a variety of neurocognitive abilities are important mechanisms of the aetiology of thought disorder symptoms. For example, the difficulties people with schizophrenia have in engaging with the environment may be due to working memory deficits, resulting in a lack of flexibility toward environmental stimuli [2]. Deficits in shifting mental set are also proposed to underlie the level of insight into their disorder that people with schizophrenia have [3], and episodes of mania in bipolar disorder are accompanied by mental set shifting deficits [49]. Schizophrenia is often accompanied by a range of behavioural issues and deficits in inhibition that are often claimed to be central to these issues. For example, deficits in inhibition are said to be deterministic of the poor planned and impulsive behaviour in schizophrenia [4]. Furthermore, deficits in a person with schizophrenia's speed of processing has been seen to mediate these broad neurocognitive deficits [50].

Ultimately, neurocognitive abilities seem to be fundamental to understanding psychopathology symptoms across Caspi et al.'s [13] internalising, externalising and thought disorder components. General deficits in neurocognitive abilities are robustly associated with a range of psychopathologies and their symptoms. It is important to remember, however, that Caspi et al.'s [13] model is ultimately a description of psychopathological behaviours that often co-occur. Caspi et al. [13] proposed that exploring how internalising, externalising and substantive *p*-factor comes to exist will require a range of measurements across biological, cognitive and environmental domains. Therefore, to examine what the hierarchical components of domains such as Caspi et al.'s [13] bifactor model represent, a mechanistic approach exploring the association between domains such as neurocognitive abilities and the factors are required.

5. A Mechanistic Approach

A mechanistic alternative to descriptive models of psychopathology comes from the Research Domain Criteria (RDoC; [51,52]). The RDoC Framework reverses Caspi et al.'s [13] top down processes to describing psychopathology by starting with the consideration of how genetic, neurological and cognitive variation can give rise to the occurrence of psychopathological symptoms. The RDoC framework has led to programmes of research that have advanced our knowledge of the mechanisms that might underlie psychopathology (e.g., [53,54]). However, the RDoC approach is also not without limitations. Kotov et al. [12,27] argue that by disregarding clinical phenotypes, and basing the exploration of psychopathology at the most basic levels, the RDoC framework has little current clinical utility. Kotov et al. [12] and Patrick and Hajcak [55] suggest that the weaknesses of both the symptomatic based hierarchical structures, such as Caspi et al. [13], and the weakness of the lower-level, mechanistically oriented RDoC framework, can be reconciled by combining the approaches. It has been suggested that joining symptomatic psychopathology structures with the RDoC constructs is likely to result in mechanisms that are measurable, consistent and explanatory of the phenotypes of psychopathology [12,55].

Linking descriptive (e.g., [13]) and mechanistic approaches (e.g., RDoC; [51]) to psychopathology requires the use of domains that are robustly associated with psychopathology at both the lower (e.g., chemical, genetic and neurological) and higher (e.g., psychopathological symptoms) levels. Neurocognitive abilities are included as one of the key domains in the RDoC system, as these abilities are associated with a wide range of psychopathology at each level of analysis (Genes, Molecules, Cells, Circuits, Physiology, behaviour and self-report; see [51,52]). Furthermore, neurocognitive abilities are also significantly associated with the internalising, externalising and thought disorder factors in Caspi et al.'s [13] correlated factors model, as well as the *p*-factor of psychopathology in the bifactor model [13]. Therefore, satisfying both criteria, neurocognitive abilities are an excellent candidate for joining the two approaches to the study of psychopathology. However, our ability to successfully link these two approaches relies on developing a thorough understanding of the meaning of *p*, and the specific factor of psychopathology. Recent literature has uncovered a range of methodological and conceptual issues that have important implications for the use of *p* as a substantive construct.

6. *p*, Substantive Factor, or Statistical Artifact?

In recent years a number of important questions and critiques have been made regarding the structural approach to psychopathology; many of these have important implications towards using these frameworks when exploring what may underpin psychopathology. Recent literature explores the question of if the *p*-factor is a substantive, meaningful construct, or rather simply a statistical artefact derived from the characteristics of the methods used. Snyder and Hankin [56] explain that the general factor of psychopathology is dependent on the characteristics of its makeup, and therefore is an inherently inconsistent construct. Lahey et al. [57] describes *p* as the "weighted average" (p. 61) of the symptoms of a sample at that point in time. This conflicts with *p* being a potentially substantive construct with a

consistent meaning and interpretation. Furthermore, Levin-Aspenson et al. [58] explored the applicability of the *p*-factor among different samples. Levin-Aspenson et al. [58] used three large data sets to conduct their exploration: (1) the National Comorbidity Survey [59], (2) Collaborative Psychiatric Epidemiology Surveys [60], and (3) the Methods to Improve Diagnostic Assessment and Services [61]. The first two being large (N = 8098 and N = 19,823, respectively) epidemiological data sets, and the third being a large data set (N = 2900) from an outpatient psychiatric hospital. The authors found bifactor models to be a good fit in each population; however, the loadings of the disorders on the *p*-factor varied extensively across the populations. Furthermore, issues have been raised regarding the indices often used to justify the *p*-factor. Greene et al. [62] assessed the possibility that the better fit generally found by bifactor models (those that include the *p*-factor) over correlated factor models (with no *p*-factor) may simply be due to fit indies unfairly biasing the bifactor models. This may mean that, even though bifactor models tend the fit collections of diagnoses and symptoms best, this may not be due to any substantive reason. Greene et al. [62] found data simulated from a correlated factors model most often better fit a bifactor model rather than a correlated factors model through which the data was created. Greene et al. [62] called for the selection of a model of psychopathology to be based on substantive interpretability and the utility of the model to facilitate the goals of the research, rather than model fit.

The applicability and substantive meaning of the *p*-factor, as well as externalising, internalising and thought disorder factors needs also to be considered *within* samples. Given that the factors of psychopathology are derived from covariation amongst of psychopathological symptoms *across* the sample, the applicability and substantive meaning of those factors will likely vary greatly for sub-groups and individuals *within* the sample. While *p* and the other factors of psychopathology might do well at summarising symptomology for the population, they may be of substantially less utility for a substantial number of individuals within that sample. This consideration means it is difficult to draw conclusions of what may underpin psychopathology on the individual and sub-group level and any conclusions made might lead us astray. For example, Caspi et al. [13] found the large majority of measures of neurocognitive ability to be significantly associated with externalising, internalising, and thought disorder factors. However, with the introduction of the *p*-factor in the bifactor model, the associations between the measures of neurocognitive ability and the internalising, externalising and thought disorder factors almost all fell to non-significant, and instead each measure of neurocognitive ability was significantly associated to the *p*-factor. This might lead us to the conclusion that neurocognitive ability has the greatest importance to psychopathology at the *p*-factor level. However, it is likely that a number of individuals in Caspi et al.'s [13] sample had a high number of psychopathological symptoms, but a low *p* score, due to, for example, a lack of general comorbidity of symptoms and a different pattern of symptoms to the mean. We might then naively assume, due to the importance of neurocognitive abilities to psychopathology seemingly being at the *p*-factor level, that neurocognitive abilities may not be important to understanding this person's psychopathology. To summarise, the primary limitations of CFA structural models are as follows: (a) it is unclear if the factors of psychopathology have, or can have, universal substantive meaning, (b) fit indices often used to champion one model over another are bias toward bifactor models, and (c) the applicability and consistency of structural models within subgroups of a population is not currently known.

Ultimately, for the *p*-factor to be useful in the exploration of neurocognitive abilities and psychopathology, a fuller understanding of the characteristics of the factor is needed. The methodological and conceptual issues of substantive *p* have led to a host of authors calling for a consensus on a definition on what the *p*-factor is, as well as an agreement on what should predict the general factor, and what the general factor should predict, in order to establish the factor as a substantive construct [29,58,62,63]. Further, other authors have argued for an alternative model to mitigate the fluidity of a general factor of psychopathology [34,64,65].

An Alternative Appraoch

The issues of developing a universal substantive *p* have led some authors to prioritise an alternative structural model, called the S-1 bifactor model [34,65,66]. The S-1 bifactor model is named as such due to it containing one less specific factor than standard bifactor models [65]. In a traditional bifactor model, each indicator loads onto the general factor, as well as one specific factor. However, in an S-1 bifactor model, a chosen set of indicators does not load onto any specific factor and only loads onto the general factor. Eid [65] describes these indictors as being the 'reference domain'. The reference domain, as it only loads onto the general factor, and 'becomes' or defines that factor. Therefore, a researcher can pre-specify precisely what the general factor represents, circumventing the issues with an undefined general factor (e.g., the *p*-factor). The variance in an S-1 model's specific factors reflects the common variance amongst the factor indicators after taking into account the general factor [65]. The reference domain, and therefore the general factor, can reflect any theoretically outstanding variable of interest [34].

Interestingly, some traditional bifactor models have ended up transforming to S-1 bifactor models unknowingly. For example, Heinrich et al. [34] showed that when Caspi et al. [13] removed the thought disorder factor from their bifactor model due to a Heywood case, they turned their model into an S-1 bifactor model, as OCD, mania and schizophrenia loaded onto the *p*-factor and no specific factor. Thought disorder, therefore, came to represent the general factor, and the *p*-factor was therefore not an indication of general psychopathology.

S-1 bifactor models may offer a useful way to explore how neurocognitive abilities are associated to psychopathology. It is possible to use a range of measures of neurocognitive abilities as direct indicators of the general factor, thereby defining its meaning [64]. This could provide information that other approaches could not. For example, it would then be insightful to examine the unique variance of each symptom indicator, as well as the variance within each specific factor, after accounting for the general (neurocognitive) factor. The S-1 approach could be used with a correlated factors model to provide more information regarding the associations of specific neurocognitive components. The S-1 bifactor approach has promise for advancing our understanding of neurocognitive abilities association to psychopathology across a sample; however, it means the rejection of a general factor of psychopathology and limitations in accounting for the heterogeneity among the associations between neurocognitive abilities and psychopathology that characterise this research. The heterogeneity of neurocognitive abilities association with psychopathology is key to developing a nuanced or mechanistic understanding of the aetiology of symptoms [18]. Therefore, it is important to consider this variation and the approaches most suitable for its exploration.

7. Heterogeneity of Psychopathology and Neurocognition

Associations between neurocognitive abilities and psychopathologies, a direct one-to-one correspondence, or perfect association, between neurocognitive abilities and the psychological, behavioural and biological components of psychopathologies has never been found. Therefore, a neurocognitive ability cannot be seen as deterministic of psychopathology. A large body of literature has explored the specific causes of disorders across biological and cognitive mechanisms. However, finding singular mechanisms with a one-to-one, deficit-diagnosis correspondence with a disorder has been elusive. For example, at the biological level, the search for specific genes with a one-to-one correspondence with a disorder has been met with limited success (e.g., [67]). The *COMT* gene, while reliably shown to be associated with a variety of disorders, does little to account for the phenotype of a disorder on an individual level [68,69]. Similarly, across each level of biological analysis, heterogeneity on an individual level is the rule rather than the exception (e.g., [70]). This means that, while certain variations may be associated with a disorder (or multiple) at a population level and may increase the risk of developing the symptoms of a disorder, that variation is not *deterministic* of psychopathology.

Cognitive endophenotype approaches have been used to attempt to uncover underlying biological mechanisms of disorders [1]. If performance on a particular neurocognitive task is seemingly associated to the genetic basis of the disorder (i.e., poor performance is seen in people with the disorder, as well as their healthy first-degree relatives), then it is intuitive to assume that the specific neurocognitive mechanisms underlying performance on that task can be deduced to a biological basis of the disorder. However, this approach has also been met by the problem of inconsistency.

Associating specific components of neurocognition with endophenotypic markers of psychopathology has been mixed. For example, greater than average perseveration errors on the Wisconsin Card Sorting Task is found for people with schizophrenia and their first-degree relatives [71,72]. However, even though the WCST is a general executive function task involving the use of updating, shifting and inhibition, there is research crediting each of these components as primarily determining the amount of perseveration errors performed on the task [73–76]. This makes deducing the biological basis of the specific neurocognitive components contributing to perseveration errors impossible. A multitude of studies have explored the neurocognitive heterogeneity of singular disorders. At a population level, there are clear general neurocognitive deficits among psychopathologies. However, at an individual level the precise neurocognitive components that are deficit range dramatically. For example, Martino, et al. [77] found that, within bipolar disorder, 38% were not deficit in any neurocognitive domain, 40% were deficit in one to two domains and 22% were deficit in three to four domains, and the disorder was not deterministic of a deficit in any particular neurocognitive domain. Raffard and Bayard [78] found similar heterogeneity in people with schizophrenia. Ninety four percent of people with schizophrenia had deficits in at least a single neurocognitive task, 27% showed deficits in two tasks 23% showed deficits in three tasks, while 23% showed deficits in four neurocognitive tasks [78]. Furthermore, functioning in these neurocognitive domains is generally not associated with duration of the illness, current psychoticism status or medication (e.g., [78]). Even when comparing disorders, deficits in particular neurocognitive domains that are able to separate the disorders are generally not uncovered [79]. The heterogeneity of the mechanisms of psychopathology has led to the call to disband the medically derived *cause model* when exploring psychopathology (e.g., [80]). However, the question of "where to from here" is still unclear.

Multiple Realisation and Psychopathology

Perhaps embracing heterogeneity in the study of neurocognitive abilities and psychopathology, rather than seeing it as an error or something that should be minimised, would lead to a greater understanding of their associations. The notion of *multiple realisation* comes from the philosophy of mind that postulates that a mental state, event or component can be determined by *multiple different* biological states, events or components [81]. It has been proposed that wide, varied physicality's can each experience the same mental state, event or component form and yet share no physical similarities. For example, it is generally accepted that a wide range of creatures such as humans, birds, molluscs and amphibians experience pain, yet these creatures often share very few physical properties [81]. Pain can therefore be multiply realised by many different physical states, events or components. Originally based to combat reductionism, the postulate of multiple realisation has been applied to many subjects, including psychopathology.

Multiple realisation is useful in explaining the biological heterogeneity of disorders. It gives us an idea with which to explain the lack of success in finding specific biological mechanisms underlying a psychopathology and provides a platform to separate mental and physical states, events or components. There has been a range of support for this concept through different methods. For example, Pavão et al.'s [82] computational work found that 154 computational models, each representing a different grouping on brain alterations, produced activity that represented the neural activity of schizophrenia.

Application of multiple realisation at the cognitive level may also provide a platform to explain the heterogeneity of neurocognitive abilities in psychopathology. Might we also extend multiple realisation to include the same set of realisers, but at various different levels of functioning? Haywood and Baughman [18] termed this proposal as the *multidimensional hypothesis.* The multidimensional hypothesis states that various different neurocognitive components, each with different ability levels (i.e., strengths and weaknesses) can explain a psychopathological phenotype equally well (see [18] for a detailed explaination].

The hypothesis posits that the overall neurocognitive ability of a person, or their susceptibility to a psychopathology, cannot be championed by a single neurocognitive component, nor can it be explained by an additive model where the ability level of each component is summed. Instead, the importance lies within the *interactions between the neurocognitive components' abilities*. Testing this hypothesis, Haywood and Baughman [18] proposed that the high amount of perseveration errors performed on the Wisconsin Card Sorting Task by people with schizophrenia and their first-degree relatives could be multiply realised by various different ability combinations among the neurocognitive components updating, shifting and inhibition. Applying computational methods, Haywood and Baughman [18] found that the performance on the task of people with schizophrenia, their first-degree relatives and control participants' could be simulated by computational models with different levels of abilities of updating, shifting and inhibition. This suggests that general neurocognitive ability, a robust endophenotype of psychopathology, may be better explained by the interactions among neurocognitive components rather than primarily by a single deficit, thus explaining the inability to find a consistent neurocognitive ability deficit throughout individuals with a certain disorder.

It is important to note that, over time, the fundamental postulates of multiple realisation have been questioned (e.g., [83–85]). It has been suggested that many cases of multiple realisation (Figure 3A) can be explained by either splitting the mental state, event or component into two or more states, events or components (Figure 3B), or merging the realisers [Figure 3C; see [86] for a summary]). Splitting is done if it is found that the mental state, event or component is better seen as multiple. Take, for example, if (M; Figure 3B) working memory is split into (M1) working memory capacity and (M2) working memory updating, we might find each mental component to be realised by separate physical properties (i.e., N1 and N2, respectively). Merging is done if the realisers are found to be the same physically (see Figure 3C). Pernu [86] provides the example that the intention to grasp an object (M; Figure 3C) can be found with the mean neural activity of some specific neuronal structures (N1 and N2). N1 and N2 in this case will be *merged*, resulting in a singularly realised (N) component. However, it seems that there are many contexts in which neither splitting nor merging can be easily applied and conform to existing empirical evidence (e.g., hunger; see [81]); in these cases, multiple realisation gives us a useful platform to understand heterogeneity.

There is also an inverse proposition of multiple realisation, namely *reverse multiple realisation* [86]. Reverse multiple realisation is the claim that the same physical states, events or components could realise different mental states, events and components. Bringing this concept to psychopathology would suggest that the same biological properties could underlie different mental disorders. Pernu [86] points out that reverse multiple realisation has support within the neuroplasticity and neural reuse literature. For example, Anderson [87] illustrates that neural circuits can be deployed, over time, for a different purpose if the need arises. Therefore, the same physical states, events or components can realise multiple different mental states, events or components.

Ultimately, the notion of multiple realisation (or reverse multiple realisation) provides a platform for questioning the relationship between neurocognitive abilities and psychopathology. Other than the preliminary evidence in support of the multidimensional hypothesis [18], little is known about the applicability of multiple realisation to solely cognitive and psychological states, events or components. That is, can a psychological or cognitive state, event or component be multiply realised by various other cognitive

or psychological states, events or components at different levels of functioning? Future research exploring neurocognitive variability in psychopathology at the individual level is needed.

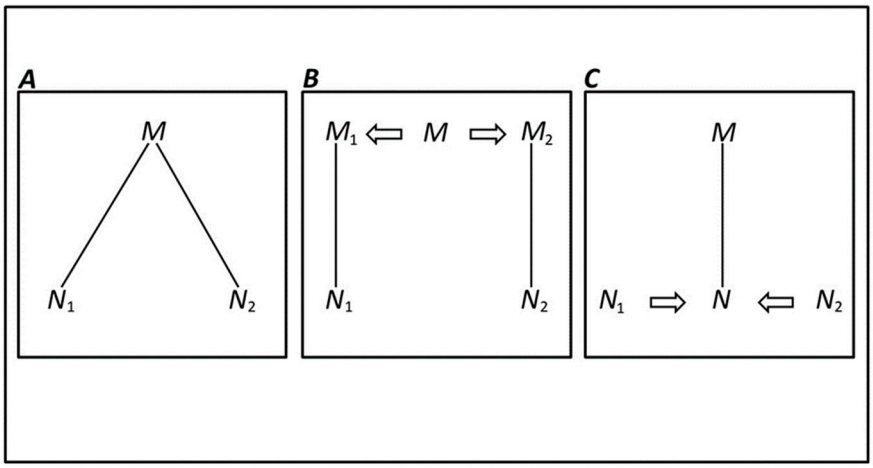

Figure 3. (**A**) displays working memory (M) being realised by two separate physical properties (N1 and N2, respectively). (**B**) shows working memory (M) being split into working memory updating (M1) and working memory capacity (M2), M1 and M2 being realised by two separate physical properties (N1 and N2, respectively). (**C**) shows the intention to grasp an object (M) being realised by the mean neural activity of some specific neuronal structures (N1 and N2), resulting in a singular unified realiser (N).

Another possibility is that the heterogeneity of neurocognitive abilities within disorders may be minimised when assessing statistically derived symptomatic components of psychopathology (i.e., internalising, externalising and thought disorder), rather than DSM defined disorders with a great level of overlap. For example, there may be clear patterns of neurocognitive ability profiles within the internalising, externalising and thought disorder components of psychopathology, and these patterns may help explain those symptom clusters and their aetiology. However, the neurocognitive heterogeneity within DSM disorders might also be seen in the statistically derived components of psychopathology, as per the multidimensional hypothesis [18].

8. The Road Forward

Structural models of psychopathology provide a promising framework to advance our understanding the relation between neurocognitive abilities and psychopathology. Finding reliable, specific associations or patterns of association, and supporting causal explanations between neurocognitive abilities and psychopathology, is unlikely if explorations continue to be based upon DSM/ICD defined disorders. Take, for example, the fact that, within the DSM, there are a total of 227 different possible symptom combinations that fulfil the criteria for a diagnosis of major depressive disorder [88]. Therefore, at the phenotype level, the symptom heterogeneity and lack of stability, as well as the comorbidity between disorders, means that consistent associations between neurocognition and DSM/ICD defined disorders are unlikely. However, as per the call of Levin-Aspenson et al. [58], a consensus around the substantive meaning of the *p*-factor is needed. The uncertainty of the meaning and applicability of the factors of psychopathology greatly limits our confidence to draw conclusions. Future research should first assess the applicability of the factors of psychopathology within sub-groups of a community sample. This will advance our understanding of how the sample derived factors of psychopathology reflect individuals and sub-groups within the sample. Future research should also assess how neurocognitive abilities are related to these factors of psychopathology *within* the sub-groups and explore association differences *between* these sub-groups. The differences in the

associations between the sub-groups may illuminate, not only the applicability and utility of the factors within sub-groups, but also provide useful knowledge on the substantive meaning of the factors and how this might differ depending on sub-group and population.

S-1 bifactor models offer a promising method of explaining neurocognitive abilities' associations to psychopathology, while mitigating the questionable substantive validity of the undefined *p*-factor [64]. The S-1 bifactor model, supplemented by the correlated factors model, seems particularly useful at the population level for examining how cognitive functioning may be associated to psychopathology. While the traditional use of the structural approaches are limited in explaining the neurocognitive heterogeneity within psychopathology, is it possible to use these approaches to elucidate potential neurocognitive performance patterns within psychopathology. If somewhat reliable patterns of associations, and causal accounts between neurocognitive components and psychopathology, are to be supported, it might be at the level of internalising, externalising and thought disorders, rather than at the level of individual disorders. However, neurocognitive abilities' association with psychopathology may also be explained at the individual level, implied by the multidimensional hypothesis [18], and the two possibilities are not mutually exclusive. The multidimensional hypothesis is also applicable at the internalising, externalising and thought disorder level, and it will be further supported if it is seen that, even within statistically derived components of psychopathology, at an individual level, multiple different profiles of neurocognitive abilities explain psychopathology equally as well. Ultimately, in our view, to progress knowledge about the underpinnings of psychopathology, future research should:

a. Further examine if a universal substantive *p* (and specific factors) could be developed the by assessment of the utility and consistency of structural models of psychopathology in subgroups.
b. Utilise the S-1 bifactor model in explorations of neurocognitive ability and psychopathology.
c. Assess if, at the population level, each of the factors of psychopathology are each best explained by a single or a small number of pattern(s) of neurocognitive component ability levels, with little variability.
d. Assess if each factor of psychopathology (e.g., internalising, externalising and thought disorder) is usefully explained at the individual level by different combinations of ability levels of the components of neurocognition (e.g., the *multidimensional hypothesis*). This would support the proposition that neurocognition's association to psychopathology, at a mechanistic level, is individual.

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