A Systematic Review on the Neurological and Psychopathological Correlates of Pica

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Abstract

Pica, the consumption of non-nutritive substances for longer than 30 days, has had several aetiologies reported. These include micronutrient deficiency, psychological and developmental disorders, and neurological and neurochemical pathologies, with a predominant focus in literature on micronutrient deficiency. Thus, a thorough exploration of the possible neurological (i.e., diagnosed conditions, neuroanatomical regions, neuropsychological profiles, neurodevelopmental disorders, neurotransmitter systems) and psychopathological (i.e., diagnosed conditions, psychological mechanism) correlates is needed. Although a recent review on the topic exists, it has not been reported on systematically. The aim of this systematic review (SR) is to firstly, provide a comprehensive overview of the existing research pertaining to neurological and psychopathological correlates of pica. Secondly, to provide a deeper understanding of pica onset and progression and to inform comorbid diagnosis and treatment of pica. Methodology of the review followed the PRISMA 2020 guidelines. Databases searched included PubMed, Scopus, Science Direct, EbscoHost (Academic Search Premier, CINAHL, Health Source: Nursing/Academic Edition, APA PsycArticles, APA PsycInfo, Medline). Methodological evaluation of studies was conducted using the Joanna Briggs Institute (JBI) Critical Appraisal Tool. An adapted JBI checklist was used for each of the study designs including case reports, case series, case control, and cross-sectional designs. 5468 journal articles were identified, 1102 articles were checked using eligibility criteria, and 15 articles were included in the review. Findings showed that the most prevalent neurological conditions correlated to pica included neurodegenerative diseases (Fronto-temporal dementia; Alzheimer's disease and Multi-infarct Dementia), acquired brain injury and stroke. The neuroanatomical regions most associated with pica included the frontal and temporal cortex as well as limbic system structures. Neuropsychological profiles of individuals with pica were in keeping with the neuroanatomical regions described and included semantic memory deficit, aphasia (Transcortical Sensory and Wernicke's) as well as cognitive difficulties following left temporal (verbal learning, memory, and reasoning) and right frontal (cognitive switching) damage. The most prevalent neurodevelopmental disorders associated with pica were Intellectual Disability and Autism-Spectrum Disorder. Successful treatment of pica mainly included serotonin inhibitors or antagonists, indicating a possible correlation between the dysregulation of serotonin neurotransmitters and pica. In addition, the most prevalent psychopathological correlates of pica included OCD, schizophrenia, and depression, with the

relief of anxiety being the most prominently reported reason for engaging in pica behaviour. Furthermore, even though these findings prove to be promising, the studies included were predominantly case report or case series, therefore a recommendation for larger scaled studies is warranted.

Keywords: *pica; neurological, psychopathological*

List of Abbreviations

ABI	Acquired Brain Injury
AD	Alzheimer's Disease
ASD	Autism Spectrum Disorder
DSM	Diagnostic and Statistical Manual of Mental Disorders
DD	Developmental Disorders
CPS	Cognitive Performance Scale
CT	Computerized Tomography
FTD	Frontotemporal Dementia
HDS-R	Revised Hasegawa's Dementia Scale
ID	Intellectual Disability
ICD-10	International Statistical Classification of Disease
JBI	Joanna Briggs Institute
KBS	Klűver-Bucy Syndrome
MDD	Major Depressive Disorder
MINI	Mini International Neuropsychiatric Interview
MMSE-J	Mini Mental State Examination – Japanese Version
MRI	Magnetic Resonance Imaging
NART	National Adult Reading Test
NDD	Neurodevelopmental Disorders
OCD	Obsessive-Compulsive Disorder
PANSS	Positive and Negative Symptom Scale
PTSD	Post-Traumatic Stress Disorder
SARI	Serotonin Antagonist and Reuptake Inhibitors
SCL-90-R	Symptom Checklist 90-Revised
SPECT	Single-Photon Emission Computerized Tomography
SSRI	Selective Serotonin Reuptake Inhibitors
TBI	Traumatic Brain Injury
TCA	Tricyclic Antidepressant

WAIS	Weschler Adult Intelligence Scale
Y-BCOS	Yale-Brown Obsessive-Compulsive Scale

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Introduction

Pica can briefly be described as a feeding disorder where individuals eat non-nutritive substances for longer than 30 days (American Psychological Association [APA], 2022). The general prevalence rate of pica is difficult to establish due to the variations in its definition over time and the low reported rates among individuals who display pica (Fawcett et al., 2016). However, pica has been predominantly reported in specific groups. Pica is commonly reported in children (Murray et al., 2018), with 12.31% children having been reported to engage in pica behaviour (4.98% recurring) compared to 5.33% (1.08% recurring) adults in population-based studies (Hartmann et al., 2018; Hartmann et al., 2022). Further pica has previously been reported as highly prevalent among patients with intellectual (ID) or developmental disabilities (DD) (Papini et al., 2023), specifically those who are institutionalised (Ashworth et al., 2008; Roberts-Harewood & Davies, 2001) as well as pregnant women (34% globally), specifically within the first trimester (Sanjari et al., 2023). Although pica is also commonly reported amongst individuals with autism spectrum disorder (ASD) (Papini et al., 2023), literature suggests that this association is more prevalent when the individual is dually diagnosed with ASD and ID (Newcomb & Hagopian, 2018). Pica has multiple reported aetiologies including micronutrient deficiency, psychological and developmental disorders, and neurological and neurochemical pathologies (Carter et al., 2004; Funayama, 2017a; Lumish, et al., 2014), with the predominant focus of studies being on micronutrient deficiency (Miao et al., 2014). There is however a dearth of systematically reviewed studies focusing on the neurological and psychopathological correlates of pica and how these two possible aetiological groups coincide within patients who present with the feeding disorder.

Literature Review

Description of Pica

The term pica stems from ‘the Latin word for magpie’**,** which is a bird that is known to eat anything (Ali, 2001, p. 205). Pica is a longstanding disorder, with the first description of it reported in 400 BCE, by the philosopher Hippocrates (Lumish et al., 2014). Pica has more recently been classified as eating non-nutritious substances (APA, 2022); however, previous researchers included substances with nutritious value in their definition, such as the ingestion of starch (Kelly, 2010). Relevant prefixes are added to the word ‘phagia’ to delineate the specific form of pica (see Table 1; Arnone et al., 2023; Bryant-Waugh et al.,

2019; Kelly, 2010). Furthermore, individuals are found to either eat one item (specific pica) or multiple items (generalized pica) (Kelly, 2010).

Table 1

Prevalent Types of Pica

Name	Material ingested
Geophagia	Clay
Pagophagia	Ice*
Coprophagia	Faeces
Amylophagia	Starch*
Acuphagia	Sharp/pointed objects
Coniophagia	Dust
Hyalophagia	Glass
Lithophagia	Stones
Xylophagia	Paper
Tricophagia	Hair, fibres, wool
Plumbophagia	Lead

Note. Materials which are indicated with * are no longer considered to be pica under the DSM-5-TR (APA, 2022)

Individuals who have pica, have previously described these cravings as being similar to someone who craves cigarettes (Beecroft et al., 1998; Hartmann & Jurilj, 2017). Even though a distraction from acting on these cravings can be useful in prolonging the behaviour, individuals with pica still feel compelled to fulfil their craving (Bhatia & Gupta, 2009; Liu et al., 2023). Diagnosis is difficult as most individuals with pica are aware that their behaviour is not socially acceptable and therefore have trouble admitting to it or informing someone of it (Liu et al., 2023). Many complications could arise from pica, which could lead to surgery or even death, through intestinal blockage, infections, and poisoning (Ali, 2001; Byard, 2014; Williams & McAdams, 2012). Life threatening pica occurs when individuals have been partaking in the eating of non-nutritive substances for years or when the substances eaten are hazardous, such as the consumption of substances containing lead (paint chips) (Bogart et al., 1995; Talbot et al., 2018; Williams & McAdams, 2012).

Diagnosis of Pica

Pica was categorized in the DSM-5-TR under the heading 'Feeding and Eating Disorders'. The DSM-5-TR includes its own independent diagnostic criteria to classify the disorder (APA,2022). The criteria stipulates that a person who has pica would partake in continuous eating of non-nutritive substances (APA, 2022). In general, such substances vary depending on the person, age and availability, but mostly include mud, clay, paper, wood, hair, chalk, charcoal and ash (Blinder, & Salama, 2008). It is important to note that most recent DSM-5-TR criteria only include non-nutritive items therefore excluding consumption of food substances such as ice (pagophagy) or raw starch (amylophagy) (APA, 2022; Miao et al., 2014)

In previous DSM criteria, pica was regarded as a disorder found in infancy and childhood but has now been recognised as a disorder that can occur in individuals of all ages (APA, 2022). Pica is predominantly found in childhood but can also be found in adolescents and adults. However, the occurrence of pica in adolescents or adulthood is a result of the disorder being undiagnosed throughout childhood unless it occurs when the individual is pregnant or suffers from iron-deficiency, neuropathology, ID, or mental health disorders (Hartmann et al., 2012). It is important to note that if pica co-occurs with another mental health disorder and if the eating behaviour is severe, then a diagnosis of pica should be made separate to the disorder (APA, 2022). Incidence of pica has however been found to decrease with age (Blinder & Salama, 2008).

A diagnosis of pica can only be made if the individual is over the age of two, partakes in continuous eating of non-nutritive substances for a month or more, and does not eat the non-nutritive substances as part of their culture, traditional practices, or social norms (APA, 2022; Hartmann, et al., 2012). Eating non-nutritious substances between the age of 18 -14 months is seen as part of typical development as children at this age learn through exploration by placing items in their mouths (Leung & Hon, 2019). This idea was also put forward by Freud as the oral stage (Al-Sawaf, 2004). If a child, however, is found to be continuing this behaviour after 18 -24 months, then developmental disability has long been reported as a potential causal factor (Baltrop, 1966; Leung & Hon, 2019).

Aetiologies of Pica

Micronutrient Deficiency

There have been many controversies surrounding the association of pica to micronutrient deficiencies. Several studies report on the association between pica and zinc or iron deficiencies, which often coexist, and may lead to anaemia (Lumish, et al., 2014; Singhi

et al., 2003). Micronutrient deficiency has been found to be the predominant cause of pica in childhood (Ganesan & Vasaukas, 2023). Studies have found that children displaying pica also had rickets, which is caused by a lack of vitamin D, and that they live in lower socioeconomic settings, and are often exposed to poverty and a restrictive availability of foods (Agarwal, 2017).

Researchers have put forward two possible causes for the association between pica and micronutrient deficiencies. The first theory suggests that a lack of micronutrients within the body may lead individuals to eat non-nutritious substances in response to the deficiency (Ali, 2001; Advani et al., 2014; Ganesan & Vasaukas, 2023). Zinc deficiency, for example, is associated with an adaption in taste and impairment in sense of taste (unable to differentiate sweet, sour, bitter, salty), which could affect eating behaviour (Kim et al., 2016; Prasad, 1996; Yanagisawa et al., 2016). The second theory suggests that eating non-nutritious substances results in a lack of zinc or iron (Srivastava, 2019). This process can firstly occur when pica substances attach to the mucosal layer within the gut, therefore prohibiting the absorption of iron or zinc within the body (Prasad, 1996; Young et al., 2011). Secondly, this process may occur when non-nutritious substances absorb the micronutrients from food which therefore does not allow for these micronutrients to be metabolized (Borgna-Pignatti & Zanella, 2016).

Neurochemical Pathologies

The neurochemical pathologies associated with pica correlates closely with the etiological associations of iron deficiency and pica. Studies have suggested that iron deficiency is associated with reduced dopamine receptors and this in turn is the reason for pica rather than the deficiency itself (Muñoz & Humeres, 2012; Volkow et al., 2017). To support this suggestion, a study done by Singh et al. (1994) indicated that when individuals with ID were given medication to improve their dopamine levels (methylphenidate) they were less likely to exhibit pica behaviour when compared to individuals with ID who did not receive sufficient treatment. Furthermore, abnormal serotonin and noradrenaline levels were found within individuals who exhibit pica (Singh et al., 1994).

It is important to note, that even though the above studies have found that the introduction of certain pharmaceutical treatments aid in the reduction of pica, no research has truly been done to highlight how these neurotransmitters are linked to pica-specific behavior. Most of the studies included are case reports and theorize that pica could be a result of an existing psychiatric diagnosis such as OCD or depression, and that treatment of the psychiatric diagnosis through pharmaceutical intervention then reduces pica symptoms (Beck et al., 2005; Gundogar et al., 2003; Stein et al., 1996). However, some studies have identified that the psychiatric condition may be treated, and pica behavior may persist (Stein

et al., 1996)

A study by Gervasini et al. (2018) found an association between dopamine pathways and feeding behavior, with dopamine D4 receptors being correlated to behaviors often accompanying eating disorders such as impulsivity, obsessive-compulsive behaviors, and anxiety, etc. In addition, a study by Lee and Lin (2010) found an association between serotonin transporter genes and eating disorders where serotonin was found to be vital in appetite regulation (increase in serotonin decreases eating and an decrease in serotonin increases eating).

Neuroanatomical Correlates

The neuroanatomical areas of the brain associated with pica has been under researched, with most of pica's neurological connection (i.e., cognitive or neurochemical) being associated with mental health disorders (Rajput et al., 2020; Schnitzler, 2022). Few researchers have explored a potential neurological cause of pica through a limited number (mostly single case design) studies to date (Beecroft, et al., 1998; Passov et al., 2011; Rohde et al., 2013).

The results of older research suggest associations between pica and frontal temporal lesions. For example, Danford and Huber (1981) found left temporal damage in monkeys and amygdala damage in cats as likely links to pica. Beercoft and colleagues (1998) also report on a 75-year-old woman who had schizophrenia and then developed pica, with the consumption of coins. Upon further examination, Computerised Axial Tomography scans reflected left frontal and right temporal lobe reduction (Beercoft et al., 1998). Another study done by Morris et al. (1989) with 33 patients with dementia showed that seven of the patients had pica. The neuropathological findings of these patients included abnormalities in the hypothalamus and medial temporal lobe. It is important to note, that these studies did not provide how these lesions were identified, how these lesions occurred, or the exact localization of the lesion.

Recent research has been undertaken by Funayama et al. (2017) in which manual tracing techniques by using morphological imaging with MRI and CT scans were used to identify lesions caused by cerebrovascular disease, traumatic brain injury (TBI) or brain tumors. The findings of their studies suggested that individuals with lesions which affected the posterior part of the left middle and inferior temporal gyri, had fewer frontal release signs, and who had severe semantic memory deficits, were likely to exhibit pica (Funayama et al., 2017).

Research on frontotemporal dementia supports the idea that damage to this neuroanatomical area results in an 80% change rate in eating behaviour and diets, with hyperorality (placing non-food items in mouth) to be the most observed change. Semantic

dementia patients were also previously found to present with changes in preference of foods (Mendez et al., 2008).

Neurodevelopmental Disorders

Neurodevelopmental disorders (NDD) can be defined as disorders which inhibit the typical development of milestones pertaining to cognitive, emotional and/or motor domains (Gilissen et al., 2014). NDD's occur due to genetic mutations which lead to dysregulation of various neurological pathways (Kumar et al., 2019). Types of NDD's associated with pica include ID and ASD, which often co-occurs (Du et al., 2018; Niemi et al., 2018).

Intellectual Disability. Intellectual disability develops during childhood and is lifelong. It is associated with complications before birth, during birth, and during childhood. Before birth complications include genetic conditions, problematic prenatal development, foetal-alcohol syndrome, and illnesses transmitted from the mother, such as HIV. During birth complications include premature birth, injuries during birth, and injuries to the developing brain due to health issues. Childhood causes include head injuries, infections affecting brain growth, seizures, and malnutrition (Johns & Adnams., 2016).

Pica is found to be the most diagnosed eating disorder found in individuals with ID with results showing pica to be significantly related to the degree of ID or DD (RobertsHarewoord & Davies, 2001). Pica has also previously been found to be more common in institutionalized individuals with ID when compared to the public (Ali, 2001). Furthermore, ID was found to be a greater risk factor for developing life threatening pica as a high morbidity rates were found in institutionalised patients with ID. Pica was also previously found to be more prevalent in institutionalized individuals with ID and autism (Bradley & Isaacs, 2006).

Thus far the speculated causes for pica within this group are primarily based on the individual not being able to identify food from non-food substances (Al-Sawaf, 2004). As ID is a DD which often occurs in childhood and is carried over into adulthood, it would be important to look at the reason for onset of pica during childhood (John & Adnams, 2016). One of the explanations for pica during childhood seems to be the result of developmental delays where the child continues eating non-nutritive substances over the age of two. As noted, the developmental delay is highly specific to Freud's oral stage or the 'hand-mouth' phase where children place various objects and substances in their mouths (Al-Sawaf., 2004; Roberts-Harewood et al., 2001).

Autism Spectrum Disorder. The most common NDD associated with pica is ASD (Bradley & Isaacs, 2006). Most of this research has been done in institutionalized settings where individuals who presented with severe ID and or ASD were the most prone to develop pica (Newcomb & Hagopian, 2018). Controversially, these studies suggest that the association of pica to ASD in these settings are due to the high rate of ID individuals who

present with ASD rather than ASD being a trigger on its own (Matson et al., 2013).

The high rates of pica within institutionalized patients with ID and ASD compared to individuals with ID and ASD outside institutions are related to the lack of emphasis placed on socialization within these institutes, as many patients are isolated from the public and rarely receive visitation from family members (Goldschmidt, 2018). The consumption of cigarettes is the most common item eaten within institutionalized patients with pica who have ID and ASD even though the individual does not have any addiction to nicotine or drugs (McGuire et al., 2007).

Pica is either seen as a challenging behaviour or a psychopathology in association with ASD. Challenging behaviours are behaviours that are not accepted culturally, isolates the individual from society, makes the individual dependent, and decreases their standard of living (Goldschmidt, 2018). Psychopathology within the context of pica and ASD refers to pica stemming from comorbid disorders such as anxiety and depression (Goldschmidt, 2018; Rajput et al., 2020; Schnitzler, 2022). As noted previously, pica can develop within individuals who present with depression or anxiety as means to self-sooth, comfort and cope with the stressors causing the comorbid disorders (Coniglio & Farris, 2021)

Psychological Disorders

Several studies have proposed the idea of pica as a comorbid disorder to mental health disorders such as obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD) and schizophrenia (Akgul, 2020; Carter et al., 2004; Rajput et al., 2020; Vanderburg et al., 2024). However, most of these studies are based on case studies or have few individuals in their participant group and do not result in much evidence for this claim, leaving the association of pica as a comorbid disorder, questionable (Matson et al., 2013).

Further studies have evaluated the definition of pica more thoroughly and have noted that a differentiation needs to be made between pica as a disorder and behaviours associated with pica (Chalker, 2017). Pica-related behaviours refer to individuals who practice pica behaviours (eating non-nutritive substances), but the primary cause of their pica behaviour is due to psychological disorders (Akgul, 2020; Chalker, 2017). For example, an individual who, as a result of anxiety, starts using pica as a coping technique. This differentiation is important as it supports the claim that pica can exist as a distinct disorder, but it could also exist as an additional behaviour to an existing psychological disorder.

Pica is also reportedly characterised by ‘impulsive and compulsive’ traits. Individuals with pica tend to display impulsivity when eating these substances and a compulsive drive to get it (Akgul, 2020), however efforts to reclassify pica within OCD diagnosis have been controversial (Jain et al., 2023)Studies on OCD and pica are inconsistent, as most researchers found associations (Akgul, 2020; Butler & Allen, 2020; Gundogar et al., 2003; Stein et al., 1996), while more outdated research did not (Gangdev & Kariuki, 1996). A single case study

by Bhatia and Gupta (2009) on depression and pica also found associations between pica and impulsive, compulsive, and obsessive traits, however it was not associated with OCD, but rather with stress and anxiety. Firstly, the patient displayed pica when presented with a stressful situation. Secondly, when the patient resisted the urge to eat non-nutritious substances it led to anxiety, which was only relieved once she had performed the behaviour. Patients with mental health disorders and pica-related behaviours are found to have reduced pica behaviour once they receive medication for the mental health disorder (Bhatia & Gupta 2009; Bhatia & Kaur, 2014; Jawed et al., 1993).

Neuropsychological Profile of Individuals with Pica

Neuropsychological assessments have barely been done on patients with pica. In their single-case study, Beecroft and colleagues (1998) undertook cognitive testing on a 75-year-old patient who had frontotemporal atrophy and pica. The patient displayed a decline in cognitive functioning, during which pica was diagnosed, compared to premorbid IQ levels. Furthermore, the patient displayed impairments in verbal learning, memory and reasoning which was consistent with left frontal brain atrophy. The patient also had impairment in cognitive switching (visual) which is consistent with right frontal brain atrophy (Beecroft et al., 1998).

More recently, Funayama et al. (2017) also assessed patients who had degenerative diseases such as Alzheimer's and Semantic Dementia, which were found to be associated with the development of the feeding disorder. To this end, associations were made between semantic memory deficits, due to brain injury specifically to the posterior part of the middle temporal gyrus, degenerative diseases, and pica (Funayama et al., 2017). Further research is needed to determine whether these frontotemporal damage and cognitive impairments are tied to pica (Beecroft et al., 1998). More studies including neuropsychological assessment of patients with pica are needed.

Similar Systematic Reviews

Database searches on the 15 December 2023 within the following search engines; EBSCOHOST (Academic Search Premier, CINAHL, Health Source: Nursing/Academic Edition, Medline, APA PsycArticles, APA PsycTests), Google Scholar and Pubmed, provided no specific systematic reviews on the neurological or psychopathological (i.e., mental health or specific mental conditions such as OCD, Schizophrenia etc.) correlates or aetiologies of pica. The search did not include grey literature and only included literature published in English. Many of the systematic reviews found on correlations of pica, focused on pica within pregnant women (Fawcett et al., 2016; Sanjari et al., 2023) and pica and micronutrient deficiencies (i.e., zinc or iron) (Ganesan & Vasaukas., 2023; Miao et al., 2014).

Only three systematic reviews were found to contain sections on neurological and

psychopathological correlates (Leung & Hon, 2019; Rose et al., 2000; Williams et al., 2022), however these articles were general overviews which included sections on epidemiology, aetiology and pathogenesis, clinical manifestations, clinical evaluations, lab findings, complications, and management of pica (see Table 2). Within the aetiology and pathogenesis sections of these reviews, neurological (i.e., middle temporal gyrus, hippocampal and cingulate gyrus) and psychopathological (OCD, ASD, ID, ADHD, Depression, Schizophrenia) links were briefly identified. However, due to the general overview of the reviews, an in-depth exploration of not only what the links/correlations are but, a) what underlines them, how they could be associated, how they overlap, and the patients experience of pica behaviours within the context of these correlations were not unpacked.

Likewise, a literature review (Schnitzler, 2022) on a similar topic to this systematic review (SR) was identified (see Table 3), however the review covered multiple aspects related to pica and did not provide a systematic review (i.e., systematic searches, inclusion/exclusion criteria) of literature. Importantly, a clear distinction was not made between studies which included patients which had iron/zinc deficiency and a neurological or psychopathological condition, which meant that a clear correlation between neurological or psychopathological conditions cannot be made in the presence of the leading cause of pica (micronutrient deficiencies).

Table 2

Systematic Reviews Including Neurological or Psychopathological Correlates of Pica

Authors	Correlates	Neurological Diagnosis	Psychopathological Diagnosis
Rose et al., 2000	Micronutrient deficiency (iron & zinc), family stress, OCD	None	OCD
Williams et al., 2022	Iron deficiency, dental pain, renal disease, sickle cell disease, developmental disorders (ASD, ID), FAS, Middle temporal gyrus	Middle temporal gyrus	Developmental disorders (ASD, ID)
Leung & Hon., 2019	Mentally handicapped, hypothalamic, and anterior cingulate gyrus lesions, ASD, ADHD, schizophrenia, OCD, depression, iron deficiency	Hypothalamic and anterior cingulate gyrus lesions	ASD, ADHD, Schizophrenia, OCD, Depression

Table 3

Comparison Between a Similar Reviewed Article and Current Systematic Review

	Current systematic review	Similar literature review
Title	• A Systematic Review of the Neurological and Psychopathological correlates of pica	• The Neurology and Psychopathology of Pica
Number of included studies	• 15	• 39
Studies which were included in both	• Funayama et al. (2017) Semantic memory deficits are associated with pica in individuals with acquired brain injury.	
Main focus	• Neurological correlates (i.e., neurological conditions; brain regions, neuropsychological profile, neurodevelopmental disorders, neurotransmitters) • Psychopathological correlates (i.e., mental disorders)	• General focus on the most common aetiology of pica (i.e., nutritional deficiency – iron and zinc) and common groups of individuals experiencing pica (i.e., pica in pregnant women). • ASD • Treatments
Methodology	• Followed a clear systematic review process with a co-rater which included inclusion/exclusion criteria, methodological checking and reference mining.	• Not a systematic review, rather a literature review of current papers on the topic. Therefore, no co-rater, no inclusion/exclusion criteria; no methodological quality checking or reference mining.
Exclusion criteria	• Patients with micronutrient deficiency because identifying neurological and psychopathological correlate in patients who have the most prevalent aetiology (zinc and iron deficiency) may skew findings.	• No exclusion criteria provide, however study included discussion of micro-nutrient deficiencies, pica in pregnant women and eating of starch and ice.

	• Excluded individuals who were pregnant and those who consumed non-edible objects due to cultural/tradition. • Excluded individuals who ate starch or ice as this was excluded as being termed as pica within the DSM-5.	
Finding chapters	• Neurological correlates of pica • Neuropsychological profile of pica • Psychopathological correlates of pica • Successful pharmaceutical treatments correlated with pica	• Pica and pregnancy • Pica in mental illness, dementia, ASD • Treatment of pica • Is pica a type of addiction?
Key main findings under chapters	Neurological correlates: • Neurodegenerative disease (Frontotemporal dementia, Alzheimer's disease), multi-infarct dementia, acquired brain injury and stroke. • Neuroanatomical regions correlated to pica were frontal and temporal cortex and hippocampus. Neuropsychological correlates: • Semantic memory deficits. • Aphasia (transcortical sensory and wernicke's) • Other correlates related to frontal and temporal regions were also noted. Psychopathological correlates:	Pica and pregnancy: • Geophagia relation to pregnancy. • Other frequent pica substances to pregnancy: raw starches and ice eating • Geophagia is a maladaptive craving induced by micronutrient deficiencies. • Geophagia and amylophagic pica may play a role in protecting the body from toxins and pathogens. Pica in mental illness: • Associated with psychiatric and developmental disorders. • Pica occurs in patients with schizophrenia, but it seems to be a rare occurrence and is often linked to comorbid OCD. Pica in dementia: • Coprophagia linked to dementias.

- Most prominent psychopathological conditions were OCD, schizophrenia, and depression.

Neurodevelopmental correlates:

- Most prominent were ID and ASD

Dual diagnosis:

- Patients had both neurological and psychopathological conditions.
- Difficulties with teasing apart whether there is a specific neurological or psychopathological correlate.

Pharmaceutical treatments:

- Most common successful treatment was SSRI's and SARI's, both of which involves serotonin.
- Pica is not an independent diagnosis from psychopathological conditions; that pica can be treated in isolation of a comorbid neurological condition (AD).

- Pica can develop as a complication of Alzheimer' disease.
- Semantic memory deficits - left middle and inferior temporal gyri.
- Pica related to alcohol-related dementia and B12 deficiency.

Pica in ASD:

- Persistence of pica beyond age 2 has been linked to developmental disorders including ASD and ID.
- . Pica could be related to sensory dysfunction, obsessive behaviour or self-injury.

Treatment of pica:

- Behavioural analysis therapy

Is pica a type of addition?

- All pica behaviours are obsessive urges.
- Addictive behaviours - dopamine motive system.

Rationale

There have been several aetiologies reported for pica as well as groups that appear vulnerable to the development of the feeding disorder (Ashworth et al., 2008; Hartmann et al., 2018; Hartmann et al., 2022; Roberts-Harewood & Murray et al., 2018; Papini et al., 2023; Roberts-Harewood & Davies, 200; Sanjari et al., 2023). However, the neurological and psychopathological correlates have not been specifically reviewed and reported on systematically (Leung & Hon, 2019; Rose et al., 2000; Williams et al., 2022). For systematic reviews to aid in understanding pica and how the feeding disorder develops within patients who do not have micronutrient deficiency, a more in-depth exploration of neurological and psychopathological correlates needs to be made.

Psychopathological links to pica has been found within the decade and neurological underpinnings have started to be highlighted in recent years. However, understanding whether pica is imbedded within the psychopathological or neurological conditions, whether it is caused by these conditions or whether it is a separate diagnosis would be important to explore. Therefore, unpacking neurological correlates by identifying the neurological diagnosis (i.e., both neurological condition as well as neurodevelopmental diagnosis), neuroanatomical regions, neurotransmitter associations and neuropsychological presentation of patients who present with pica would be beneficial. Further, unpacking psychopathological correlates, by not solely identifying which conditions are most likely to be correlated with pica, but also which underlining psychological reasons (presented by patients) for engaging with pica behaviour would be beneficial. Lastly, unpacking pica within patients with dual diagnosis (i.e., both neurological and psychopathological conditions) would further be important in understanding whether neurological or psychopathological conditions are better linked to pica. All these explorations would not only provide the neurological and psychopathological conditions which clinicians should most likely consider when patients present with pica, but also provide practitioners with a better understanding of how these conditions relate to pica and provide researchers with gaps which need further investigation.

Aims and Objectives

The overall aim of the study was to conduct a systematic review (SR) which identified which neurological and psychopathological conditions are mostly correlated to pica. The main objectives of conducting the SR were to 1) outline the neurological conditions (neurological and neurodevelopmental diagnosis), neuroanatomical regions, neuropsychological sequalae and neurotransmitters found in patients with pica; 2) outline the psychopathological conditions as well as the psychological mechanism reported by patients with pica which contributes to engaging in pica behaviour; 3) present pica in

patients who have dual diagnosis of both neurological and psychopathological conditions and 4) identify possible gaps in research.

Method

Procedure

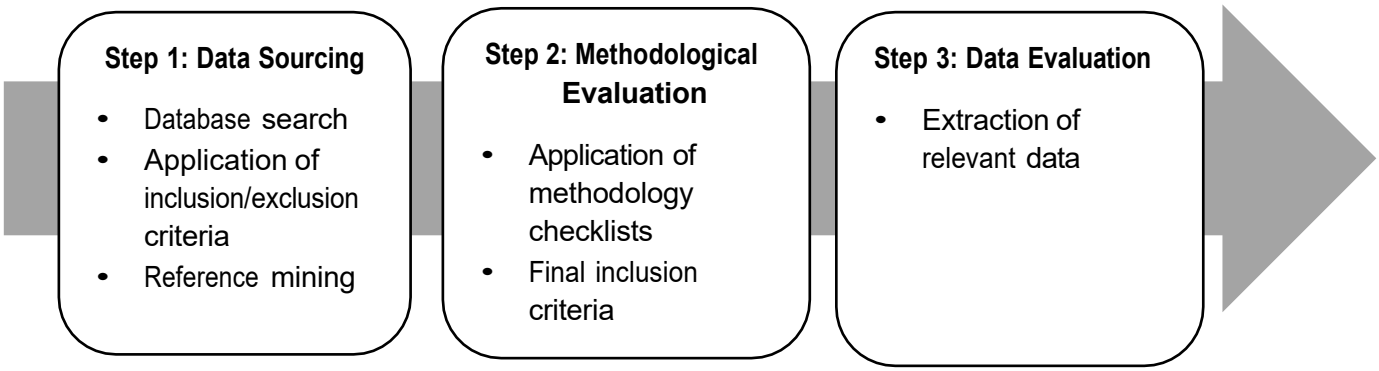
The protocol for the study followed the guidelines recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement and will be structured as per the PRISMA 2020 checklist (see Appendix A). The protocol for the study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on the 07 December 2022 (ID: CRD42022382256). It is important to note that due to the focus on COVID-19 registrations, the PROSPERO team have provided registration for the study without checking eligibility.

Literature Search Methods

The SR follows the steps outlined in Figure 1. Each of these steps are elaborated on thereafter.

Figure 1

Systematic Review Steps



Step 1: Data Sourcing

Database Search. An initial literature search was conducted by myself (LF) and my co-rater (SR; a Neuropsychology Master's degree candidate at the University of Cape Town, Psychology Department) using the following databases: PubMed, Scopus, Science Direct, EbscoHost (Academic Search Premier, CINAHL, Health Source: Nursing/Academic Edition, APA PsycArticles, APA PsycInfo, Medline). Appropriate keywords and MeSH terms were created for each database to find the

most suitable articles based on the study aims of identifying the neurological and psychological correlates of pica. Boolean phrases were added to combine keywords and MeSH terms to create the final searches for each database. Each final search set for every database is outlined in Table 4.

Table 4

Final Search Sets per Database

Database	Search Set
Pubmed	((("Pica"[Mesh]) OR (pica [Text Word])) AND ((((("Neuropsychology"[Mesh]) OR (neuropsychology[Text Word] OR neuropsychological[Text Word])) OR (("Neurology"[Mesh]) OR "Psychology"[Mesh])) OR (neurology[Text Word] OR psychology[Text Word]))) NOT (pregnancy)
Scopus	(((pica) AND (neuropsychology OR neurology OR psychology) AND NOT birds))
Science Direct	(((pica) AND (neuropsychology OR neurology OR psychology) AND NOT birds AND NOT posterior inferior cerebellar artery))
EbscoHost	(((pica) AND (neuropsychology OR neurology OR psychology)))

Note. The term pica is derived from the Latin name of the bird 'magpie' which translates to pica pica. Therefore, 'NOT birds' is included in the search set for Scopus and Science Direct as many articles about the magpie bird was included in the results of the search (Ali, 2001, p. 205).

The initial literature search, which was conducted on the 09 September 2022 (including a search of all articles using the search sets in Table 4 published up until 09 September 2022) by me (LF) and SR independently, produced the same number of articles for each database searched. Citations for all articles were exported to Mendeley (version 1.19.8), which is a reference software tool. Hereafter, the articles were uploaded onto Rayyan, which is a software program used to assist researchers conducting systematic reviews (Ouzzani et al, 2016). Duplicate articles were deleted using a function on Rayyan.

Application of Eligibility Criteria. Articles were included based on the following criteria: articles 1) were based on the final search sets for their given database (i.e., neurological and/or psychological links to pica), 2) were written in English; 3) were based on research that were conducted on human participants; 4) included individuals/participants over the age of 18 months; 5) referred to specific types of pica by including terms ending in 'phagia'; 6) were peer-reviewed. The reasons for the above inclusion criteria include the following: 1) due to the vast number of aetiologies/mechanisms/causes pertaining to pica, a

broad search of any neurological or psychological correlate will be included; 2) I am only fluent in English and therefore including articles which are written in other languages might be incorrectly interpreted; 3) due to the number of animal studies pertaining to pica (Bradshaw et al., 1997; Firyal., 2007; Nikvand et al., 2018; Takeda et al., 1993; Tharwat & Al-Hawas, 2023), only studies which include human participants will be included; 4) according to the DSM-5-TR criteria, only individuals above the age of 18 months can be diagnosed with pica; 5) varying types of pica based on what individuals digest are often termed by words ending in 'phagia', therefore articles which included these terms instead of the general term 'pica' should also be included; 6) to ensure articles followed ethical procedures and were methodologically well written.

Articles were excluded based on the following criteria: articles 1) included individuals/participants who were diagnosed with pica based on cultural practice/tradition or during pregnancy; 2) included individuals/participants diagnosed with pica and who had micronutrient deficiency (i.e., iron and zinc). The reasons for both the above exclusion criteria are that the SR's focus is on neurological and psychopathological correlates of pica, therefore for the study to produce literature which solely focuses on these two domains, all other aetiologies/mechanisms/causes/links needed to be excluded.

Article Selection According to Inclusion Criteria. The abstracts of the articles were then reviewed using Rayyan by both reviewers (LF and SR) following the application of the inclusion/exclusion criteria above. Rayyan provides the following categories for coding each article being considered for the review: 'included', 'excluded' or 'maybe'. For each category a reason could be provided. Initially, the reviewers (blind to each other's decisions) coded each article as one of the three categories independently and provided a reason for the 'excluded' articles. Once sorted, the reviewers discussed the articles within each category and came to a consensus on the articles within the 'maybe' category on whether it would be 'included' or 'excluded'. Where disputes could not be resolved, these could be discussed with my supervisor (LSB).

The full text of the articles within the 'included' category were then reviewed independently by both reviewers (blind to each other's decisions) once again applying the inclusion/exclusion criteria to the article content as some of the criteria could not be ascertained through the abstract alone. A final consensus was then reached by both reviewers on the articles which fell within each category pending the methodological evaluation.

Reference Mining. For a thorough search to be conducted, the reference list of articles that met inclusion criteria were reviewed for other articles that could be relevant to the study. The articles which met the inclusion criteria for the study, were included and added to the list of articles for the current study.

Step 2: Methodological Evaluation

A methodological evaluation based on the final list of included articles was conducted using the Joanna Briggs Institute (JBI) Critical Appraisal Tool. The JBI Critical Appraisal Tool is a peer reviewed tool used to assess the methodological quality of each article included by ascertaining the risk of bias within the article design, conduct and analysis before articles are finally included in systematic reviews (Munn et al., 2020). The JBI Critical Appraisal Tool includes a set of questions which could be answered with 'no', 'yes', 'unclear' or 'not applicable', responses. Even though this tool is a checklist, it could also be used as a scale (Barker et al., 2023). The tool was designed to be design specific, therefore providing a set of specific questions for each type of study design commonly included in systematic reviews. For this SR the JBI checklist for case reports, case series, control studies, cross-sectional study designs were used (see Appendix C).

Case report study designs reports yield low internal and external validity (Gagnier et al.,2013). Therefore, the JBI checklist is aimed at assessing the descriptive qualities of the case report studies and the quality thereof will be reported on. The other included study designs included in the SR (i.e., case series, case control, cross-sectional) questions are divided into three main methodological evaluation domains. These domains include 1) *internal validity*, 2) *comprehensiveness of reporting* and 3) *statistical conclusion validity* (Barker et al., 2022). *Internal validity* can be defined as how well a cause-and-effect relationship between an exposure and the outcome can be predicted to be true (Slack & Draugalis, 2001). *Comprehensiveness of reporting* pertains to the efficient quality of information reported in a study (Stone et al., 2019). Inefficient reporting may lead to difficulties when assessing for internal validity (Stone et al., 2019). *Statistical conclusion validity* is obtained when appropriate analysis is used which leads to adequate conclusions being drawn (García-Pérez, 2012). These domains and the questions pertaining to each of them will be further unpacked below.

Case Reports. The JBI checklist for case report studies includes eight questions (Moola et al., 2020). Descriptive qualities which were assessed within the JBI case report checklist include description of the Q1) participants demographic characteristics, Q2) diagnostic

timeline, Q3) current diagnosis, Q4) diagnostic tests Q5) and treatment, Q6) post-intervention clinical condition, Q7) unexpected events and Q8) whether conclusions can be drawn (Gagnier et al., 2013; Moola et al., 2020).

Furthermore, due to the large number of case reports included within this SR, the CARE checklist was used as an additional, more in-depth evaluation. Case reports are useful accounts of detailed medical history, treatment plans and patient accounts, which is important for inclusion within the SR, however they yield difficulties with assessing validity and reliability (Quintão et al., 2020). The CARE checklist was developed as a framework that aims to aid thorough, detailed, and complete representation of a good case report (Riley et al., 2017). The CARE checklist includes 30 questions, which are divided into the following domains: title, keywords, abstract, introduction, patient information, clinical findings, timeline, diagnostic assessment, therapeutic intervention, follow-up and outcomes, discussion, patient perspective, and informed consent (Riley et al., 2017). The checklist is used as a guide when conducting or assessing the quality of case reports, by indicating a tick for 'yes' or a cross for 'no' to each of the questions provided. There is no cut off scores, however lower numbers of 'yes' indicates that the case reports are less transparent and complete (Riley et al., 2017).

Case Series. The JBI checklist definition of a case series design includes an article in which participants with a specific outcome are selected for inclusion, whether exposed or unexposed (Dekkers et al., 2012). For the case series design, the JBI checklist had 10 questions (Moola et al., 2020). These questions were divided into three domains, namely *internal validity*, *comprehensiveness of reporting* and *statistical conclusion validity* (Barker et al., 2023).

For the first domain, being *internal validity*, the JBI checklist assessed methodological quality through evaluating participant selection bias (Q1: 'whether clear criteria for inclusion were included'; Q4: 'whether consecutive inclusion for participants were maintained' and Q5: 'whether complete inclusion for participants were maintained') and bias in measurement of outcomes (Q2: 'whether the condition was measured in a standard and reliable way' and Q3: 'were valid methods used for the identification of the condition') Barker et al., 2023).

For the second domain, being *comprehensiveness of reporting*, methodological quality was assessed through Q6) 'clear reporting of demographics', Q7) 'clinical information', Q8) 'outcomes', and 9) 'location of site'. The third domain, being *statistical*

conclusion validity, was assessed through Q10) 'whether the statistical analysis used, was acceptable' (Barker et al., 2023).

Case-Control Studies. For the case control studies, JBI checklist had 10 questions (Moola et al., 2020). The questions within the JBI checklist for case control studies assessed two broad domains, namely *internal validity*, and *statistical conclusion validity* (Barker et al., 2023).

The first domain, being *internal validity*, the methodological quality was evaluated by assessing bias related to confounding factors (Q1: 'whether groups were comparable', Q2: 'appropriately matched', Q6: 'whether confounding factors were identified' and Q7: 'controlled for'), selection bias (Q3: 'whether the same criteria were used for both cases and controls'), bias related to classification of exposure (Q5: 'whether exposure was measured in the same way for both cases and controls' and 8) 'whether it was measured in a standard, valid and reliable way'), measurement bias (Q8: 'whether outcomes were assessed in a standard, valid and reliable way for both cases and controls') and bias related to temporal precedence (Q9: 'whether the exposure period was long enough') Barker et al., 2023).

The second domain, being *statistical conclusion validity*, relates to Q10) 'whether appropriate statistical analysis was used by assessing whether appropriate relationships were drawn between variables to arrive at given conclusions' (Barker et al., 2023).

Cross-Sectional Studies. For cross-sectional study designs, the JBI checklist contained 8 questions (Moola et al., 2020). The questions within the JBI cross-sectional studies checklist assessed three domains, namely 1) *internal validity*; 2) *comprehensiveness of reporting* and 3) *statistical conclusion validity* (Barker et al., 2023).

The first domain, being *internal validity*, was assessed by checking for selection bias (Q1: 'whether inclusion criteria was defined'), bias related to classification of exposure (Q3: 'whether exposure and Q7: outcomes measured in sustainable, reliable way'), bias related to measurement outcome (Q4: 'were objective and standard criteria use for measurement of condition') and bias related to confounding factors (Q5: 'were confounding factors identified' and Q6: 'were measures put in place to mitigate said factors'). The second domain, being *comprehensiveness of reporting*, was measured by checking Q2) 'whether the studies included descriptive details of participants and setting'. The third domain, being *statistical conclusion validity*, was assessed by checking Q8) 'whether statistical analysis was appropriate' (Barker et al., 2023).

Each article included was independently assessed by both reviewers using the JBI Critical Appraisal Tool checklist for each study design. Articles were given a 'yes' if the question posed was met, a 'no' if the question posed was not met, an 'unclear' if the reviewer was uncertain of whether the question was answered or not and 'n/a' if the question does not pertain to the article (i.e., case reports and case series does not tend to include statistical analysis). The reviewers then came to a consensus after discussing all differences between evaluations. Therefore, complete agreement was achieved. The CARE checklist was used as an additional evaluation tool for case reports and was therefore only used by the main reviewer (LF).

According to the JBI checklist articles risk evaluation could be grouped as high (50% or below), moderate (50%-70%) or low (above 70%) (Goplen et al., 2019). Final inclusion criteria included whether articles achieved between moderate to low-risk evaluation scores, indicating that articles were methodologically sound.

Step 3: Data Extraction

An excel spreadsheet was used to categorise the information found in the articles to ensure that the information reported on for each article was consistent and relevant. The headings within the excel spreadsheet included the following information: authors, year of publication, title of study, journal of publication, study design, sample size, sample characteristics, participant diagnosis, material ingested, measures used, results reported, possible limitations and recommendations.

Statistical Data Analysis

Inter-rater reliability was investigated using Cohen's Kappa, which was used to access the level of agreement across the JBI methodological quality checklists (case report, case series, case control and cross-sectional) of all included articles, between the two primary reviewers (LF and SR).

Ethical Considerations

The study has been ethically approved by the Research Ethics Committee of the University of Cape Town, within the Department of Psychology (reference number – PSY2020-010; see Appendix B).

Transparency

To ensure transparency was upheld, the systematic review (SR) was sent to PROSPERO for review before commencement.

Bias

Bias within the conduction of the SR was controlled for by ensuring that an additional reviewer (LB) was included and consulted whenever disputes between the primary reviewers

took place.

The SR holds a bias of solely including published articles in English, therefore excluding all research which may have been conducted in non-western settings in which the primary language is not English. The articles included within the SR therefore mainly includes research conducted within populations that were predominantly English, unless a transcribed article was published. As the primary language of the reviewers was English, the SR could not avoid this bias due to the possibility of incorrect interpretation, however it is important that it is recognized.

The search terms used only accounted for the term 'pica' and did not include words ending with 'phagia', which, as stated above, is often the suffix for the names of varying types of pica (see Table 1). Therefore, there is a bias within the search terms of the SR towards articles which include pica as a general condition, rather than specific types of pica.

Handling of Data and Reporting of Findings

The SR focuses on vulnerable population groups and therefore special attention needs to be made when reporting results. The SR has considered the use of stigmatizing language, and that certain terminology may be perceived as harmful to the vulnerable populations being discussed.

Results

Step 1: Data Sourcing

Database Search

The initial database search conducted by both research reviewers, provided a total of 5468 articles. Duplicates were then removed, providing a final article count of 1102. The number of articles provided by each database is provided in Table 5 below.

Table 5

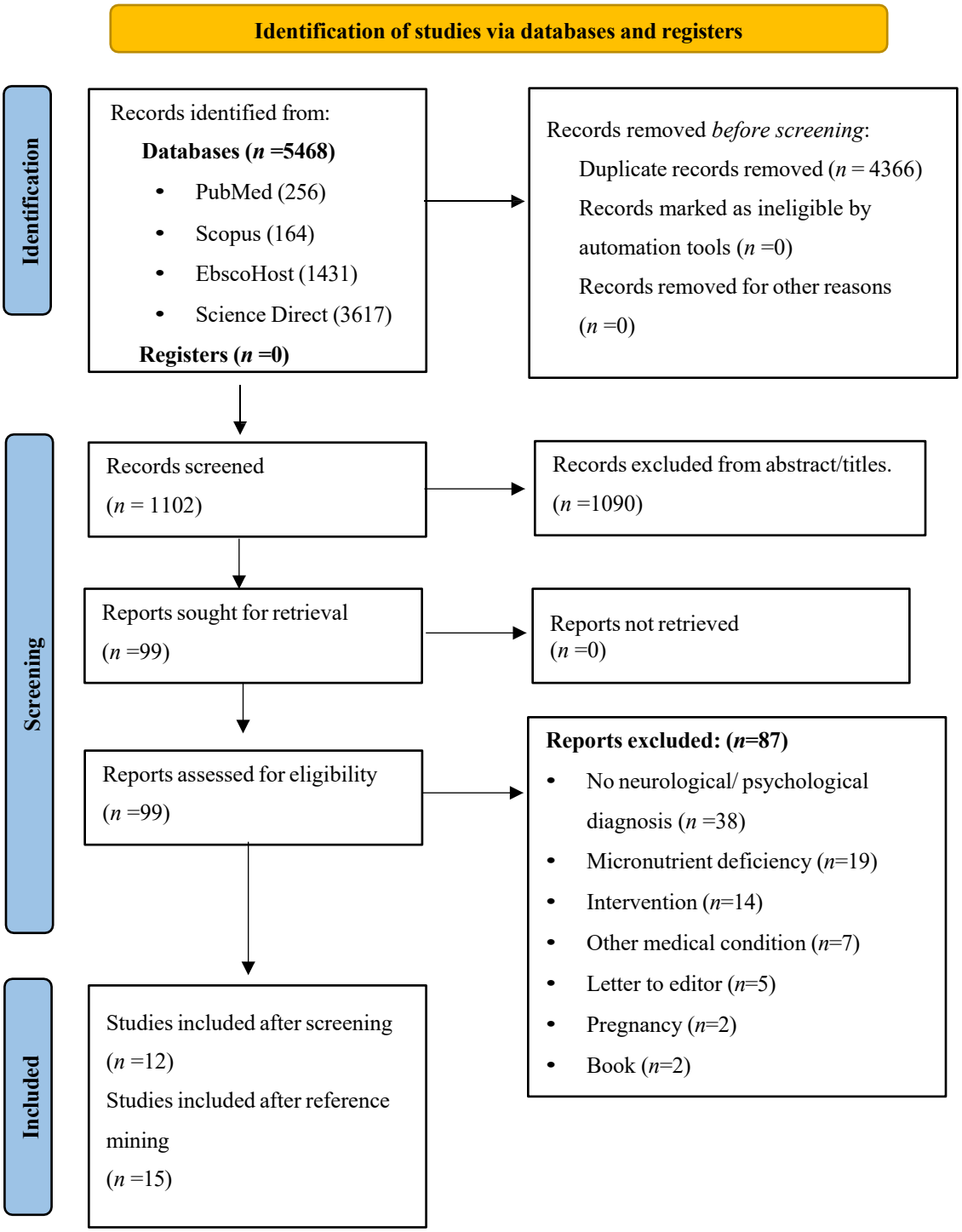
Number of Articles per Database

Database	Articles
PubMed	256
Scopus	71
EbscoHost	760
Science Direct	15
Total	1102

Note. EbscoHost search included Academic Search Premier, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Health Source: Nursing/Academic Edition, APA PsyArticles, APA PsyInfo, Medline)

Figure 2

PRISMA 2020 Flow Diagram (Included Articles of Databases only)



Application of Inclusion/ Exclusion Criteria

The total number of articles found in the databases were then reviewed independently by both reviewers, using the inclusion/exclusion criteria. An abstract search of each article was done using Rayyan. After an initial review of the (*n* =1102) articles by both reviewers, 982 were *excluded*, 81 were *included* and 39 were coded as *maybe*. Both reviewers then discussed the articles within the '*maybe*' category and a consensus was reached in which 21 articles were excluded and 18 were included, resulting in an overall inclusion of 99 articles. Both reviewers independently conducted a full-text article search of the included articles (*n*= 99) using the exclusion criteria. The full-text search yielded 87 articles to be excluded and 12 to be included.

A large number of articles were excluded based on multiple factors, namely articles which included 1) Posterior Inferior Cerebellar Artery (PICA); 2) animal studies; 3) intervention studies; 4) no neurological or psychological diagnosis; 5) other medical conditions which arose due to ingestion of non-edible objects; 6) ice-eating (i.e.,pagophagia); 7) micronutrient deficiency (i.e., iron or zinc); 8) pregnant women; 9) consumption of non-edible objects due to cultural practice and 10) these being non-English.

Reference Mining

A final search of the reference lists of the 12 included articles were examined by both reviewers to find any other eligible studies. A total of three additional articles were found and included, making the final number of articles 15 (See table 6 below). Figure 2 (PRISMA 2020 flow diagram) provided below, outlines a summary of each step taken to reach the final number of articles.

Table 6

Articles with Neurological and/or Psychopathological Correlates Included for Review

Author	Year	Journal	Title	Correlates
Kinnell	1985	British Journal of Psychiatry	Pica as a Feature of Autism	Neurological
Stein et al	1996	South African Medical Journal	Pica and the Obsessive-Compulsive Spectrum Disorders	Psychopathological
Beecroft et al	1998	International Journal of Geriatric Psychiatry	Case Report: An Unusual Case of Pica	Both
Matson & Bamburg	1999	Journal of Developmental and Physical Disabilities	A Descriptive Study of Pica Behaviour in Persons with Mental Retardation	Neurological
Gundogar et al	2003	General Hospital Psychiatry	Is Pica in the Spectrum of Obsessive-Compulsive Disorders?	Psychopathological
Dumaguing et al	2003	Journal of Geriatric Psychiatry and Neurology	Pica in the Getriatric Mentally Ill: Unrelenting and Potentially Fatal	Both
Beck & Frohberg	2005	The International Journal of Psychiatry in Medicine	Coprophagia in an Elderly Man: A Case Report and Review of the Literature	Both
Baheretibeb et al	2008	Clinical Case Studies	The Girl Who Ate her House – Pica as an Obsessive-Compulsive Disorder	Psychopathological
Ashworth et al	2008	Journal of Mental Health Research in Intellectual Disabilities	Prevalence of Correlates of Pica Among Adults with Intellectual Disability in Institutions	Neurological

Bhatia & Gupta	2009	World Journal of Biological Psychiatry	Pica Responding to SSRI: An OCD Spectrum Disorder	Psychopathological
Josephs et al	2016	Journal of Neurology	Coprophagia in Neurologic Disorders	Both
Funayama et al	2017	Behavioural Brain Research	Semantic Memory Deficits are Associated with Pica in Individuals with Acquired Brain Injury	Neurological
Osuji & Onu	2019	Clinical Nutrition ESPEN	Feeding Behaviors among Incident Cases of Schizophrenia in a Psychiatric Hospital: Association with Dimensions of Psychopathology and Social Support	Psychopathological
Fields et al	2021	PEDIATRICS	Pica, Autism, and Other Disabilities	Neurological
Kanamori et al	2021	Frontiers in Psychiatry	Successful Combination Therapy of Trazodone and Fluvoxamine for Pica in Alzheimer's Disease: A Case Report	Neurological

Note: The term 'both' under the correlate heading refers to articles which contain both neurological and psychopathological correlates of pica.

Step 2: Methodological Evaluation

Each of the included articles (*n*=15) was assessed independently by both reviewers using the specified checklists outlined by the JBI critical appraisal tools for each study design. Both reviewers came to a consensus regarding the results of the methodological evaluations for each included article until complete agreement was met. The JBI methodological checklists used for the included articles (*n*=15) were checklists for case reports (*n*=5), case series (*n*=3), case control studies (*n*=3) and cross-sectional studies (*n*=4). Each checklist included specified questions pertaining to the given study design. All included questions aimed to assess internal validity, risk of bias, comprehensiveness of reporting and statistical analysis. Due to the large number of included case reports (*n*=5), the CARE checklist was applied in addition to the JBI case report checklist, to assess the validity, applicability, and transparency of the case reports. The CARE checklist was only completed by the primary rater as an additional means to check descriptive quality of case reports.

Cohen's kappa (κ) was run to evaluate the agreement between the two raters, using each checklist question for all articles included across all study types (i.e., case reports, case series, case control and cross-sectional) resulting in N=132 subjects (i.e., all checklist questions in total). Each checklist question was used as a separate decision. Results indicated that inter rater reliability was high between the two raters across all checklists, $\kappa = .82$, $SE = 0.051$ (95% confidence interval from 0.71 to 0.91), $p < .001$.

Tables 7-11 outline the outcome of each rating per article for each study type. All articles were included, regardless of the methodological evaluation outcome due to the overall limited number of studies initially included/appropriate for review. The risk evaluation for each of the articles was described as high (50% and below), moderate (50% - 70%) or low (above 70%). Articles which demonstrated high risk (i.e., 50% and below) were reviewed with caution.

Case Report Design Methodological Quality Evaluation

CARE Checklist. As Table 7 demonstrates, three of the case studies achieved a rating of 70% and above (i.e., 70%, 80% and 83.33%), indicating that these case studies included sufficient descriptive information pertaining to most of the domains included. Two of the case studies, however achieved scores of 50% and 56.67% indicating a lack of quality reporting. Specifically, the study of Beercroft et al. (1998) did not report any information pertaining to follow-up and outcome of the patient. In addition, the study by Beck and Frohberg (2005) demonstrated insufficient information pertaining to multiple domains (i.e.,

introduction, clinical findings, diagnostic assessment, therapeutic intervention and follow-up and outcome).

Table 7

Summary of Case Report Methodology Checklist (CARE) for Included Case Report Studies (n=5)

Author	Title	Keywords	Abstract	Introduction	Patient information	Clinical findings	Timeline	Diagnostic assessment	Therapeutic intervention	Follow-up and outcome	Discussion	Patient perspective	Informed consent	Total Score	%	Risk
Baheretibeb et al., 2008	1/1	1/1	3/4	1/1	3/4	1/1	0/1	3/4	3/3	4/4	4/4	0/1	0/1	24/30	80	Low
Beck & Frohberg., 2005	1/1	1/1	4/4	0/1	4/4	0/1	0/1	1/4	1/3	2/4	1/4	0/1	0/1	15/30	50	High
Beecroft et al., 1998	1/1	1/1	3/4	0/1	4/4	1/1	0/1	2/4	2/3	0/4	3/4	0/1	0/1	17/30	56.67	Mod
Bhatia & Gupta 2009.	1/1	1/1	4/4	1/1	4/4	1/1	0/1	1/4	2/3	3/4	3/4	0/1	0/1	21/30	70	Mod
Kanamori et al., 2021	1/1	1/1	4/4	1/1	4/4	1/1	0/1	2/4	3/3	3/4	4/4	0/1	1/1	25/30	83,33	Low
Total per item	5/5	5/5	18/20	3/5	19/20	4/5	0/5	9/20	11/15	12/20	15/20	0/5	1/5			

Note: Some domains above have multiple questions, therefore the total within each block represents the number of questions which received a point. Risk percentage calculated using the following formula: Total score x 100 ÷ 30 = % risk.

Total Quality Across JBI Case Report Checklist. As demonstrated in Table 8, four out of the five case reports included in SR presented with a low-risk methodological quality (Beecroft et al., 1998; Bhatia & Gupta, 2009; Kanamori et al., 2021), with the highest score being 100% (Baheretibeb et al., 2008). One of the five case reports included, however presented with a high-risk methodological evaluation (i.e., 50%) (Beck et al., 2005). The large number of case reports falling within the low-risk range, is indicative of the case report studies holding similar methodological evaluation outcomes. However, it is important to note that case reports yield difficulties with assessing validity and reliability therefore the overall

low-risk methodological evaluations of these case report studies should be interpreted with caution as it most likely portrays good descriptive qualities rather than good study design. One aspect most lacking in comprehensive description across the case report articles included (Q7), was whether adverse events were clearly described within the articles.

Quality Score for Each Item on JBI Case Report Checklist. As highlighted in Table 9 it is evident that one case report (Baheretibeb et al.,2008) provided sufficient descriptions of Q1) 'participant demographic characteristics', Q2) 'diagnostic timeline', Q3) 'current diagnosis', Q4) 'diagnostic tests', Q5) 'treatment', Q6) 'post-intervention clinical condition', Q7) 'unexpected events' and Q8) 'whether conclusions can be drawn' (Moola et al., 2020). The descriptive criteria which were not included in the remaining four case reports, pertained to Q7) 'whether unexpected events were identified and described'. Beck and Frohberg (2005), provided the least comprehensive descriptive case report, as information pertaining to Q5) 'whether interventions were clearly described', Q6) 'what the post-interventions were' and Q8) 'was their clear take away points' from the study was not included. Therefore, the Beck and Frohberg (2005) study demonstrated the highest risk (50%) and was the least comprehensive case report.

Table 8

Summary of Case Report Methodology Checklist (JBI) for Included Case Report Studies (n=5)

Authors	1. Were patient's demographic characteristics clearly described?	2. Was the patient's history clearly described and presented as a timeline?	3. Was the current clinical condition of the patient on presentation clearly described?	4. Were diagnostic tests or assessment methods and the results clearly described?	5. Was the intervention(s) or treatment procedure(s) clearly described?	6. Was the post-intervention clinical condition clearly described?	7. Were adverse events (harms) or unanticipated events identified and described?	8.Does the case report provide takeaway lessons?	Total Score	%	Risk
Baheretibeb et al., 2008	✓	✓	✓	✓	✓	✓	✓	✓	8	100	Low
Beck et al., 2005	✓	✓	✓	✓	-	X	X	X	4	50	High
Beecroft et al., 1998	✓	✓	✓	✓	✓	n/a	-	✓	6	85,7	Low
Bhatia & Gupta 2009	✓	✓	✓	-	✓	✓	X	✓	6	75	Low
Kanamori et al., 2021	✓	✓	✓	✓	✓	✓	X	✓	7	87,5	Low
Total pet item	5/5	5/5	5/5	4/5	4/5	3/4	1/5	4/5			

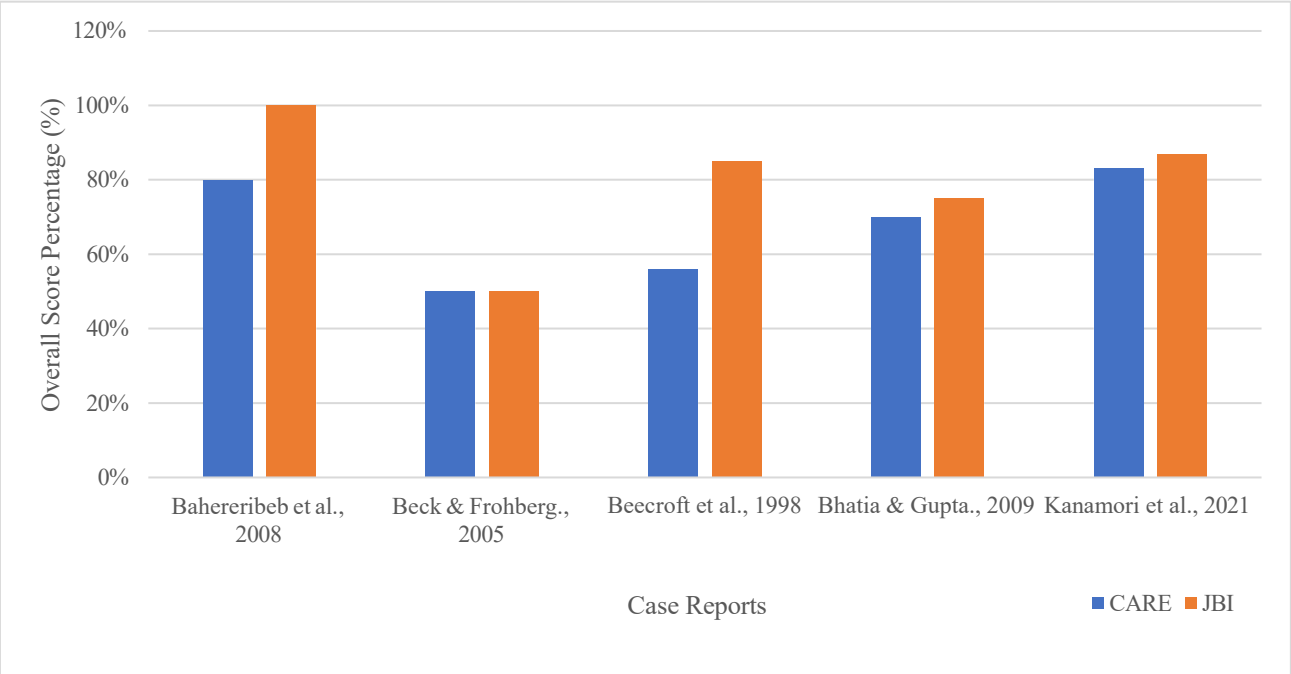
Note: ✓ indicates that item was met. X indicates that the item was not met. n/a indicates that item was not applicable and (-) indicates that item was unclear due to the descriptive nature of case reports, following the guidelines presented by JBI checklist. Risk percentage calculated using the following formula: Total score x 100 ÷ total number of questions = % risk.

Overall Comparison of CARE and JBI Checklist for Case Reports. As demonstrated in Figure 3, most of the case report studies displayed similar results between the CARE and JBI checklist proportionally. However, two studies demonstrated a discrepancy between its CARE (56.6%) and JBI (85.7%) checklist results. The first study was Baheretibeb et al. (2008), which resulted in 80% on CARE and 100% on JBI checklist, both falling within the low-risk range. The second study was Beecroft et al. (1998), which resulted in 56.6% on CARE and 85.7% on JBI checklist, falling within the moderate and low risk range respectively. The discrepancy, across both checklists, is a result of the larger range of questions pertaining to various descriptive domains within the CARE checklist. For Baheretibeb et al. (2008), CARE questions pertaining to the inclusion of a clear abstract, timeline of patient's history, patient perspective of their experienced account were additional sections which caused discrepancy between the two checklist outcomes. For Beecroft et al.

(1998) questions pertaining to follow-up and outcome of patient results such as 'clinician and patient – assessed outcomes when appropriate', 'important follow-up diagnostic and other test results', 'intervention adherence and tolerability – how was it assessed' and 'adverse and unanticipated events' (Riley et al., 2017).

Figure 3

Overall Comparison of CARE and JBI Checklist Results for Case Reports



Case Series Design Methodological Quality Evaluation

Total Quality Across Case Series Studies. As demonstrated in Table 9, three case series articles were included, one which demonstrated a high risk (i.e., 44,4%) (Dumaguing et al., 2003) and two which demonstrated a moderate risk (55,5%) (Gundogar et al., 2003; Stein et al., 1996) in methodological quality. This indicates that the case series articles included showed evidence of limited quality design, conduct and analysis, which signifies high risk for low internal validity and reliability.

Quality Score for Each Item for Case Series Studies. With regards to *internal* criteria by indicating which

institution the patients were selected from, the diagnosis of the patients included and a description of the patients' diagnostic progression. With regards to Q4) consecutive and Q5) complete inclusion, none of the studies indicated that all the patients within the given institution selected from, presented with the outcome measured (i.e., pica). Rather, it was indicated that a specific number of patients were chosen to be included (i.e., three patients from an outpatient unit with pica were selected to be in the study).

With regards to bias in measurement of outcomes, two of the three case series studies (Gundogar et al., 2003; Stein et al., 1996) provided a Q2) clear description of the measurement of the condition, therefore done in a Q3) standardised and reliable way. Further, the above-mentioned case series studies included diagnosis based on the DSM-IV criteria for diagnosis of Axis I disorders (i.e., OCD) as well as MRI and CTb scans for the diagnosis of brain related injury and neurodegenerative diseases, which would be considered reliable and validated measures. However, one study (Dumaging et al., 2003) only included sufficient description of how the condition was measured for one patient. Even though the study mentioned psychiatric diagnosis for the other patients, no clear indication of the measure used for diagnosis was provided. It is important to note, that none of the case series studies included a measure for the diagnosis of pica.

As indicated in Table 10, all three case series studies presented with *comprehensiveness of reporting*. All studies included Q6) descriptions of patients' demographics (i.e., age and sex) as well as appropriate clinical information (i.e., diagnosis, progression, treatment). However, none of the case series studies included information pertaining to the Q9) demographics of the clinic in which patients were recruited, therefore making it difficult for other researchers to ascertain whether the sample used would be comparable. In addition, all three case series studies provided each Q7) patient's treatment plan and highlighted Q8) whether the treatment was successful or not by outlining which symptoms have resolved and which were still present.

Statistical conclusion validity could not be assessed as Q10) no statistical analysis was used for any of the case series included due to the descriptive nature of each of the cases.

Table 9

Summary of Case Series Methodology Checklist (JBI) for Included Case Series Studies (n=3)

	Internal Validity					Comprehensiveness of Reporting.				Statistical Conclusion Validity			
Authors	1. Were there clear criteria for inclusion in the case series?	2. Was the condition measured in a standard, reliable way for all participants included in the case series?	3. Were valid methods used for identification of the condition for all participants included in the case series?	4. Did the case series have consecutive inclusion of participants?	5. Did the case series have complete inclusion of participants?	6. Was there clear reporting of the demographics of the participants in the study?	7. Was there clear reporting of clinical information of the participants?	8. Were the outcomes or follow up results of cases clearly reported?	9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	10. Was statistical analysis appropriate?	**Total Score**	**%**	**Risk**
Dumaguing et al., 2003	✓	X	-	X	X	✓	✓	✓	X	n/a	4	44,4	High
Gundogar et al., 2003	X	✓	✓	X	X	✓	✓	✓	X	n/a	5	55,5	Mod
Stein et al., 1996	X	✓	✓	-	-	✓	✓	✓	X	n/a	5	55,5	Mod
Total per item	1/3	2/3	2/3	0/3	0/3	3/3	3/3	3/3	0/3	0/0			

Note: ✓ indicates that item was met. X indicates that the item was not met. n/a indicates that item was not applicable and (-) indicates that item was unclear due to the descriptive nature of case reports, following the guidelines presented by JBI checklist. 'Mod' refers to moderate risk. Risk percentage calculated using the following formula: Total score x 100 ÷ total number of questions = % risk.

Case Control Design Methodological Quality Evaluation

Total Quality Across Case Control Studies. As indicated in Table 10, the three case control studies demonstrated varied methodological quality, ranging from low risk (i.e., 90%) (Funayama et al., 2017), moderate risk (i.e., 70%) (Fields et al., 2021) and high risk (i.e., 33,3%) (Kinnel, 1985). It is evident that the case control study which posed the highest risk (Kinnel, 1985) presented with poor methodological quality and will be interpreted with caution. The most common bias across the case control studies included 1) bias to exposure and measurement in which (Q4) pica was not measured in a standard, valid or reliable way as most of the studies did not include a clear description of how the patients received the diagnosis. In addition, the 2) classification of exposure bias was also commonly present within the articles in which (Q8) outcomes such as comorbid diagnosis (ASD) were not assessed in a standard or

reliable way due to the lack of professional clinical expert diagnosis.

Quality Score for Each Item for Case Control Studies. With regards to *internal validty* (bias related to confounding factors, selection bias, bias related to classification of exposure, measurement bias and bias related to temporal precedence), one of the case control studies (Funayama et al., 2017) met all the applicable criteria of the checklist (i.e., one criterion was non-applicable) demonstrating that internal validity was upheld. Similarly, Fields et al. (2021) met most of the criteria, however demonstrated bias related to classification of exposure and measurement bias Q5) due to the use of tools which are Q8) not standardized. For example, observer reporting (i.e., Autism Diagnostic Observation Schedule) was used to diagnose ASD and self-administered forms and telephonic interviews were used to diagnose pica, instead of the DSM criteria or at least considering these alongside other tools. The study therefore demonstrated a possibility of over or under reporting of symptoms, therefore compromising objectivity. The study by Kennel (1985) demonstrated bias related to confounding factors (Q6) no clear confounding factors highlighted nor Q7) strategies to combat them), bias to exposure and measurement bias (Q8) no clear method of measuring/ diagnosing pica was provided). The study therefore demonstrated poor internal validity. All three case control studies did not include treatment however focused on prevalence and correlation; therefore, Q9) exposure of interest, which pertains to the associated link between exposure to treatment and outcome of said treatment, could not be assessed.

Regarding *statistical conclusion validity*, both Funayama et al. (2017) and Fields et al. (2021) studies applied Q10) appropriate statistical analyses to ascertain study conclusions. However, Kinnel (1985) did not apply any statistical analyses to derive study conclusions.

Table 10

Summary of Case Control Methodology Checklist (JBI) for Included Case Control Studies (n=3)

	Internal Validity								Statistical Conclusion Validity				
Authors	1.Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	2.Were cases and controls matched appropriately?	3.Were the same criteria used for identification of cases and controls?	4.Was exposure measured in a standard, valid and reliable way?	5.Was exposure measured in the same way for cases and controls?	6.Were confounding factors identified?	7.Were strategies to deal with confounding factors stated?	8.Were outcomes assessed in a standard, valid and reliable way for cases and controls?	9.Was the exposure period of interest long enough to be meaningful?	10.Was appropriate statistical analysis used?	**Total Score**	**%**	**Risk**
Funayama et al., 2017	✓	✓	✓	✓	✓	✓	✓	✓	n/a	✓	9	90	Low
Fields et al., 2021	✓	✓	✓	X	✓	✓	✓	-	n/a	✓	7	70	Mod
Kinnel., 1985	✓	✓	✓	X	X	X	-	X	n/a	X	3	33.3	High
Total per item	3/3	3/3	3/3	1/3	2/3	2/3	2/3	1/3	0/0	2/3			

Note: ✓indicates that item was met. X indicates that the item was not met. n/a indicates that item was not applicable and (-) indicates that item was unclear due to the descriptive nature of case reports, following the guidelines presented by JBI checklist. 'Mod' refers to moderate risk. Risk percentage calculated using the following formula: Total score x 100 ÷ total number of questions = % risk.

Cross-Sectional Design Methodological Quality Evaluation

Total Quality Across Cross-Sectional Studies. As indicated in Table 11, two of the studies (Matson & Bamburg., 1999; Osuji & Onu., 2019) maintained a low risk (i.e., 75% each) and two of the studies (Ashworth et al., 2008; Josephs et al., 2016) maintained a moderate risk (i.e., 62.5% and 60%). The overall shortcomings of the cross-sectional studies pertained to (Q5) whether confounding factors were identified and (Q6) whether these confounding factors were strategically accounted for. Overall, the cross-sectional studies demonstrated varied quality pertaining to design, conduct and analysis, however internal validity (Q5 and Q6) was the main shortcoming within the overall methodological evaluation of the cross-sectional studies included.

Quality Score for Each Item for Cross-Sectional Studies. Regarding *internal validity* (selection bias, bias related to classification of exposure, bias related to measurement outcome and bias related to confounding factors), one study (Ashworth et al., 2008) demonstrated selection bias due to insufficient clarity on Q1) inclusion and exclusion criteria. Some criteria for Josephs et al. (2016) were non-applicable such as Q3) whether exposure or Q7) outcomes were measured due to the acquisition of data for the study (i.e., medical records were examined and used). All cross-sectional studies included demonstrated bias related to confounding factors as none of the studies clearly identified possible Q5) confounding factors or Q6) means to mitigate them.

Regarding *comprehensiveness of reporting*, all cross-sectional studies included Q2) sufficient information regarding participants (i.e., diagnosis, ethnicity, age, gender etc.) and location (i.e., time period and where the study took place). Therefore, all studies included provided comprehensive reporting.

Regarding *statistical conclusion validity*, three studies (Ashworth et al., 2008; Matson & Bamburg, 1999; Osuji & Onu, 2019) included Q8) use of appropriate statistical analyses for the conclusions made within the studies. One study (Josephs et al., 2016) did not make use of statistical analysis as the study was descriptive.

Table 11

Summary of Cross-sectional Methodology Checklist (JBI) for Included Cross-Sectional Studies (n=4)

	Internal Validity		**Comprehensiveness of Reporting**				**Statistical Conclusion Validity**				
Authors	1. Were the criteria for inclusion in the sample clearly defined?	2. Were the study subjects and the setting described in detail?	3. Was the exposure measured in a valid and reliable way?	4. Were objective, standard criteria used for measurement of the condition?	5. Were confounding factors identified?	6. Were strategies to deal with confounding factors stated?	7. Were the outcomes measured in a valid and reliable way?	8. Was appropriate statistical analysis used?	**Total Score**	**%**	**Risk**
Ashworth et al., 2008	X	✓	✓	✓	X	X	✓	✓	5	62.5	Mod
Josephs et al., 2016	✓	✓	n/a	✓	-	-	n/a	n/a	3	60	Mod
Matson & Bamburg., 1999.	✓	✓	✓	✓	X	X	✓	✓	6	75	Low
Osuji & Onu., 2019	✓	✓	✓	✓	X	X	✓	✓	6	75	Low
Total pet item	3/4	4/4	3/4	4/4	0/4	0/4	3/4	3/3			

Note: ✓ indicates that item was met. X indicates that the item was not met. n/a indicates that item was not applicable and (-) indicates that item was unclear due to the descriptive nature of case reports, following the guidelines presented by JBI checklist. 'Mod' refers to moderate risk. Risk percentage calculated using the following formula: Total score x 100 ÷ total number of questions = % risk.

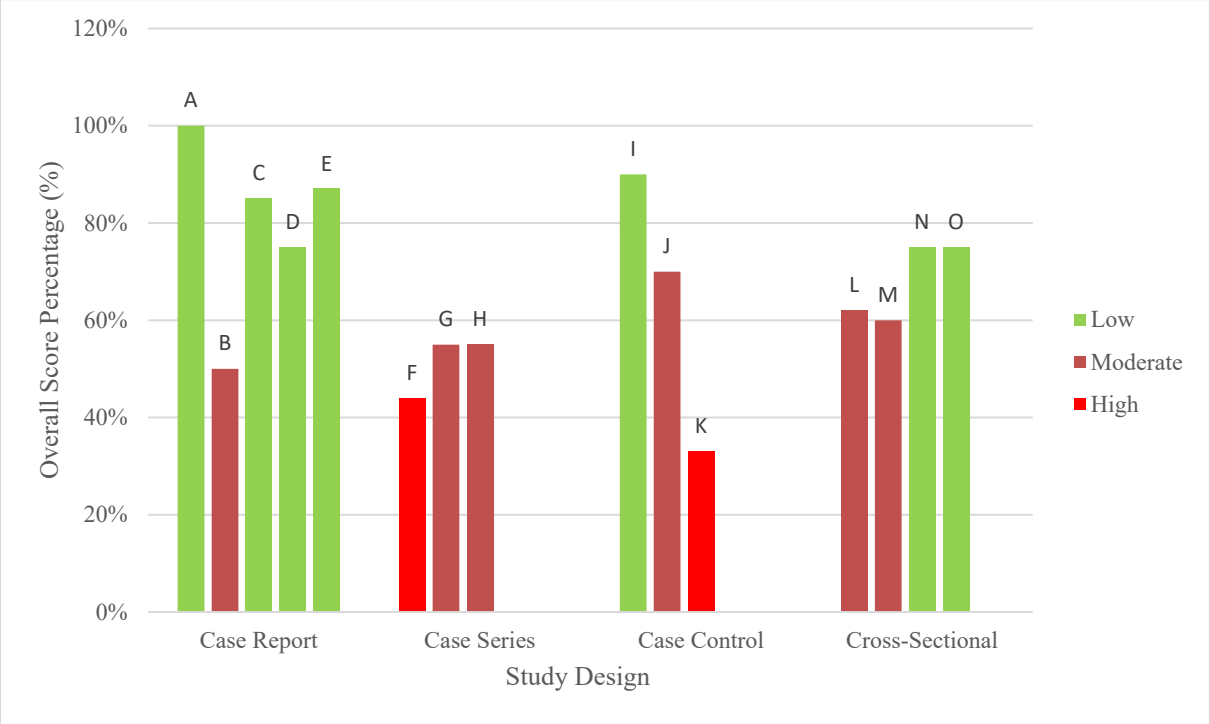
Overall Quality on JBI Checklist Across Studies

Overall percentage scores were calculated for each study using the total score of each study type. As demonstrated in Figure 4, overall percentage scores ranged from 100% to 33.3% across studies. The studies which maintained the highest scores were case reports, with the case series studies scoring the lowest when comparing them collectively. As previously mentioned, assessing methodological quality for case reports is difficult due to the descriptive nature as well as the limited participant size of case reports. Therefore, Figure 4

highlights that the case reports included demonstrated good descriptive qualities rather than good reliability and validity.

Figure 4

Overall Scores of all Included Studies (JBI Checklist) Across Study Designs



Note: Each bar represents an article which was included in the SR. Each letter refers to the articles listed as: A (Baheretibeb et al., 2008), B (Beck et al., 2005), C (Beecroft et al., 1998), D (Bhatia & Gupta, 2009), E (Kanamori et al., 2021), F (Dumaguing et al., 2003), G (Gundogar et al., 2003), H (Stein et al., 1996), I (Funayama et al., 2017), J (Fields et al., 2021), K (Kinnel, 1985), L (Ashworth et al., 2008), M (Josephs et al., 2016), N (Matson & Bamburg, 1999), O (Osuji & Onu, 2019).

Step 3: Data Extraction

The data extracted from the articles included in the SR in terms of the neurological and psychopathological correlates are detailed in Table 6 above. Table 6 outlines the citation information (i.e., author, year of publication, journal name and title) and whether the articles contribute towards neurological, psychopathological correlates of pica or both for each of the included articles. Articles that have been categorised as neurological if pica is correlated to 1) neurological diagnosis, 2) neuroanatomical region, 3) neurodevelopmental disorder or 4) neuropsychological/cognitive profile. Articles that have been categorised as psychopathological if pica is correlated to a diagnosed mental health disorder. Tables 12-16 outlines the design and characteristics, materials ingested,

diagnostic measures (including a discussion on the lack of consistency in the measure of pica) and outcomes, diagnostic findings, and successful pharmaceutical treatment of all included articles, respectively. As some included articles include both neurological and psychopathological correlates, extracted information have been discussed together.

Design and Sample Characteristics

Table 12 outlines the design characteristics of each article which reported on neurological and psychopathological correlates of pica. Given that most of the included articles were case reports and case series, the main contributions to this SR were detailed case descriptions and prevalence studies, rather than large participant study designs (e.g., randomized control trials).

Due to the varied study designs included, samples sizes ranged from single case reports (*n*=1) to larger samples in the cross-sectional (*n*=14 to *n*=1008) and case control (*n*=19 to *n*=4739).

Participants within the studies ranged from 30- to 68-month-olds (toddlers and young children) to adults (i.e., 94 years old), with some studies solely focused on children (Fields et al., 2021), some solely on adults (Ashworth et al., 2008), and others including combined samples of child and adult participants (Stein et al., 1996; Funayama et al., 2017).

Study sites for participant recruitment neurological correlates of pica (*n*=3) included a general hospital (*n*=1), cognitive dysfunction clinic (*n*=1) and Mayo Clinic Sciences computerized database (*n*=1). Sites for participant recruitment within studies which focused on participants with predominantly psychopathological correlates to pica (*n*=12), were mainly from psychiatric facilities (i.e., clinics or hospitals; *n*=7), while other recruited participants from nursing homes/residential care (*n*=2) and general hospitals (*n*=1). Two studies' recruitment methods were unspecified.

Table 12

Design and Sample Characteristics for Articles Included

Author	Study Type	Sample	Sample Size(*n*)	Recruitment
Kanamori et al.	Case Study	80 y/o female	1	Hospital admission
Beecroft et al.	Case Study	75 y/o female	1	Residential care
Bhatia et al.	Case Study	35 y/o female	1	-
Beck et al.	Case Study	77 y/o male	1	Nursing home.
Baheretibeb et al.	Case Study	17 y/o Ethiopian female	1	Medical outpatient department of a general hospital.
Dumaguing et al.	Case Series	79, 69 and 94 y/o males	3	Geriatric unit of a state mental hospital.
Gundogar et al.	Case Series	15 y/o and 47 y/o females; 15 y/o male	3	-
Stein et al.	Case Series	18, 34 and 45 y/o females; 83 y/o male; 8 y/o boy	5	Outpatient anxiety disorder and OCD clinics
Josephs et al.	Cross-sectional	20-88 y/o (M = 55) Male: n=6; Female: n=6	12	The Mayo Clinic Health Sciences-computerized clinical database
Matson et al.	Cross-sectional	30 male and 15 female Age range 17 to 80 y/o (mean age 48.11 years).	45	Institutional settings
Osuji et al.	Cross-sectional	Age range 18-60 y/o. The majority (58.7%) were females, single (63.6%), had high school education (56.0%) and were employed (57.8%).	206 (incident cases)	Federal Neuropsychiatric Hospital
Ashworth et al.	Cross-sectional	Male (62.0%) On average, 51.6 years of age (24.2 to 89.6, SD = 9.4)	1008 (census-level data)	Specialized Institutions
Funayama et al.	Case Control	Predominantly males.	11 (pica)	Cognitive Dysfunction Clinic

		Age range: 16-88 y/o	8 (hyperorality)	
Fields et al.	Case Control	Children 30 to 68 months of age.	1426 (ASD) 1735 (DDs) 1578 (POPs)	Special education and clinical sources (ASD and DD) Randomly selected birth records (POP's)
Kinnell	Case Control	Autistic subjects: mean age 31.3 (range 9- 76 years). Down's syndrome subjects: mean age 42.1 years (range 21-75 years)	140 (70 ASD and 70 Down Syndrome)	Case records

Note. ASD: Autism Spectrum Disorder, DD: children with other developmental difficulties, POP: general population controls

Material Ingested

Table 13 outlines the materials ingested across patients within included studies. Some materials ingested included weeds, detergents, coins, chalk, mud, sand, toilet paper, cigarette buds, etc. Across all the studies, which included various patients with differing diagnoses, the type of material ingested was not consistently related to a specific diagnosis. The only non-edible object which seemed to be commonly digested by patients with ID was faeces (Beck et al., 2005; Dumaguing et al., 2003; Josephs et al., 2016). In addition, Matson & Bamburg (1999) identified cigarette buds as being the most digested object amongst patients with ID living in institutionalized settings (*n*=28).

Table 13

Materials Ingested

Author	Materials Ingested
Kanamori et al.	Weeds and dishwashing sponge
Beecroft et al.	Vitamin C tablets, coins, nuts, wire, plastic, 'purple hearts', Bob Martin's dog conditioning powder and dried flowers.
Bhatia et al.	Chalk
Beck & Frohberg	Faeces
Baheretibeb et al.	Mud
Dumaguing et al.	Toilet paper, napkins, Styrofoam cups, crayons, medications. Faeces, fingernails, hair, urine. Cigarette butts, faeces, and garbage.
Gundogar et al.	Cigarettes, Hair
Stein et al.	Sand, faeces, chalk, newspaper
Josephs et al.	Faeces
Matson & Bamburg	Cigarette butts, small pieces of paper, clothing, bed linens and towels, faeces.
Osuji & Onu	-
Ashworth et al.	-
Funayama et al.	Daily necessities: toothpaste, soap, sponge, shampoo, face lotion, laundry detergent, bathing powder, antiseptic solution, air freshener, cotton paper, toilet paper, diapers.
Fields et al.	-
Kinnell	Paper, grass, mud, plastic objects, and coins.

Note. (-) indicates that no materials were specified within the article, however these articles did refer to the individuals having pica and eating non-nutritious substances.

Table 14
Diagnostic Measures and Outcomes

Author	Measure	Outcome of Measure
Kanamori et al.	Revised Hasegawa's Dementia Scale (HDS-R) CT scan	HDS-R score was 20/30. Head CT shows selective hippocampal atrophy which progressed compared with 3 years earlier. Her medial temporal atrophy seemed asymmetrical (R>L). Diagnosis of Alzheimer's Disease.
Beecroft et al.	CT scan National Adult Reading Test (NART): premorbid IQ WAIS: current intellectual functioning	CT evidence of frontotemporal atrophy most marked on the left in the temporal lobe and on the right in the frontal lobe. Premorbid full-scale IQ=106 (average range) Current full-scale IQ=86 (low average range)
Bhatia & Gupta	DSM-IV-TR assessment	Diagnosis of depression with relational problems and pica
Beck & Frohburg	Medical records	Medical records
Baheretibeb et al.	DSM-IV assessment	Diagnosis of pica and OCD (moderately severe).
Dumaguing et al.	DSM-IV assessment Slosson Intelligence Test (IQ) MRI and CT scan	Pt 1: Schizoaffective disorder and mild cortical atrophy following a stroke. Pt 2: Dementia praecox with mild developmental delay. MRI showed extensive gliosis surrounding the lobotomy defects and mild to moderate cerebrocortical and cerebellar atrophy. Diagnosis of multi-infarct dementia. Pt 3: Paranoid schizophrenia. CT scan revealed generalised cortical and cerebellar atrophy and a small basal ganglia lacunar infarct. Diagnosis of Alzheimer's-type dementia.
Gundogar et al.	Yale-Brown obsessive-compulsive scale (Y-BOCS) Symptom checklist 90-revised (SCL-90-R) DSM-IV assessment	Pt 1: Y-BOCS score was 14/ SCL-90-R score was 2.10 Pt 2: Y-BOCS score was 19/ SCL-90-R score was 1.5 Pt 3: Y-BOCS score was 30/ SCL-90-R score was 2.30
Stein et al.	Medical records were looked at (Phenomenology, neurobiology sand pharmacotherapy data).	4 cases: Patient diagnoses with OCD and impulse control disorder In one patient pre-treatment SPECT revealed multiple perfusion defects, including the frontal cortex bilaterally, but also the temporal cortex bilaterally, occipital cortex bilaterally, left parietal cortex, left caudate and both sides of the thalamus (more pronounced on the left). Post-treatment SPECT revealed

		improvement in frontal cortical perfusion, as well as in most other previously abnormal areas. The perfusion defect in the right occipital area remained unchanged.
Josephs et al.	Demographic, clinical, neuroimaging and neuropathological data were abstracted from patient medical records.	Coprophagia was associated with dementia in six patients, developmental delay in two, and each with seizures, steroid psychosis, frontal lobe tumor, and schizoaffective disorder. Brain imaging in the six patients with dementia, showed moderate-to-severe medial temporal lobe atrophy, as well as mild frontal lobe atrophy. Autopsy examination was performed in one patient and revealed frontotemporal lobar degeneration pathology.
Matson & Bamburg	Questions About Behavioural Function (QABF) The Matson Evaluation of Social Skills in Persons with Severe Retardation (MESSIER)	Most of the persons in the study engaged in pica for non-social reasons. Individuals without pica displayed a significantly larger number of social skills. The most prevalent diagnosis with pica disorder included stereotypic movement disorder and autistic disorder.
Osuji & Onu	Mini International Neuropsychiatric Interview (MINI) Socio-demographic questionnaire Positive and Negative Symptom Scale (PANSS) Multi-dimensional Scale of Perceived Support (MSPSS)	Socio-demographic characteristics of the 206 schizophrenic patients. Schizophrenia patients aged 18-30 constituted 43.7% of all the participants. The majority (58.7%) were females, single (63.6%), had high school education (56.0%) and were employed (57.8%). Inappropriate feeding behaviours were seen in 13.2% of the patients, with the most common inappropriate feeding behaviour as abnormal food preparation (46.4%). Minority of them had pica (14.3%).
Ashworth et al.	interRAI Intellectual Disability (interRAI ID): Measures of CPS (The Cognitive Performance Scale) ADL-H (The Activities of Daily Living Hierarchy Scale)	Persons residing in the 3 specialized institutions had an unspecified cause (i.e., mental retardation, 34.5%) or other genetic cause (53.2%) of ID. Only a minority of individuals had a diagnosis of Down Syndrome (8.7%) and autism (3.6%). Persons most often had severe ot very severe levels of cognitive impairment. Overall, 21.8% engaged in pica.
Funayama et al.	Mini-mental state examination Frontal release signs, semantic memory deficits, changes in eating behaviours were compared: Pica-related behavioural features.	Compared to the hyperorality group the pica group had more severe semantic memory deficits and fewer frontal release signs, whereas there was no significant difference in changes in eating behaviours.
Fields et al.	Pica prevalence ratios adjusted for sociodemographic factors.	Pica was higher in children with ASD (23.2%) and DD (8.4%) and within the following subgroups: ASD with ID (28.1%), ASD without ID (14.0%), DD with ID (9.7%), DD with ASD characteristics (12.0%), and DD with both ID and ASD characteristics (26.3%).
Kinnell	None	None

Diagnostic Tools

Table 14 outlines the diagnostic tools reported across studies. The data extracted pertaining to which diagnostic tools were used for pica as well as the tools used to measure the neurological (i.e., neurological conditions, neuropsychological profiles, and neurodevelopmental conditions) and psychopathological conditions will be outlined below.

Pica Diagnoses. Almost half of the included studies (*n*=7) did not provide a clear description of the measure used for the diagnosis of pica (Beck & Frohberg, 2005; Beecroft et al., 1998; Funayama et al., 2017; Josephs et al., 2016; Kanamori et al., 2021; Kinnell, 1985; Stein et al., 1996). These studies either provided a case description of the patient (*n*=4) or made use of medical records (*n*=3) in which reference to pica was made, however a measure of pica was not provided. The absence of a measure may be due to incomplete medical records, poor case description or no clear tool of measurement for the diagnosis of pica.

Some of the included studies (*n*=5) made use of the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)* for the diagnosis of pica (Baheretibeb et al., 2008; Bhatia & Gupta, 2009; Dumaguing et al., 2003; Gundagar et al., 2003; Matson & Bamburg, 1999), while other studies made use of the DSM-IV to exclude other probable eating disorders (Osuji & Onu, 2019). Further, there were two studies which made use of other questionnaires for the diagnosis of pica (Fields et al., 2021; Osuji & Onu, 2019). Osuji and Onu (2019) used a *socio-demographic questionnaire* to assess 'nutritional variables' under which eating of non-nutritional substances was included. Fields et al. (2021) used the *Child Behaviour Checklist*, a parent report form, in which participants were identified as having pica by mothers' responses to the question "child eats or drinks things that are not food-not including sweets" (Field et al., 2021, p. 3). One study, Ashworth et al. (2008), made use of *direct observation* across three days. A diagnosis of pica was given if patients placed non-nutritious items in their mouth during the three-day observation period or if staff indicated that they had pervious concerns regarding a patient who displayed pica behaviours.

Neurological Conditions. Fives studies (Beecroft et al., 1998; Dumaguing et al., 2003; Josephs et al., 2016; Kanamori et al., 2021; Stein et al., 1996) made use of neuroimaging tools such as *computerized tomography (CT)*, *magnetic resonance imaging (MRI)* and *single-photon emission computerized tomography (SPECT).* These tools were used to aid in the diagnosis of neurological conditions (i.e., neurodegenerative diseases, strokes, regions of atrophy) and to ascertain perfusion. The diagnosis of these neurological conditions was used to determine whether there was an association between these conditions and pica,

and therefore not as direct diagnostic assessment of pica per se. Stein et al. (1996) used SPECT to assess perfusion pre and post pharmaceutical treatment to identify whether said treatment aided in diminishing pica.

Neuropsychological Profile. Some studies assessed cognitive functioning within patients to either assist with the neurological diagnoses (Ashworth et al., 2008; Kanamori et al., 2021) or to determine whether certain cognitive impairments were associated with pica (Beecroft et al., 1998; Funayama et al., 2017).

Kanamori et al. (2021) used the *Revised Hasegawa's Dementia Scale (HDS-R)*, which is a useful tool for screening of dementia (Chen et al., 2014). Questions aim to assess orientation, working memory, immediate recall, and verbal fluency. This tool was used to supplement imaging for diagnostic purposes (Chen et al., 2014).

Ashworth et al. (2008) used the *Cognitive Performance Scale (CPS)*, which can be found within the *interRAI Intellectual Disability (interRAI ID)*, to measure cognitive performance in patients with ID. The CPS contains four items which assesses 1) short-term memory, 2) decision-making, 3) expression, and 4) self-performance in eating, and answers are scored between 0 (intact) and 6 (severe impairment) (Martin et al., 2007). Within the study, the CPS was used only as a means of assessing the severity of ID in patients who did not have a severity level within their medical records (21.1% of patients).

Beecroft et al. (1998) used the *National Adult Reading Test (NART)* to determine premorbid intellectual functioning (IQ) in a patient with cognitive decline. The tool is considered a reliable measure and consists of 50 questions in which a patient is asked to read various words with non-typical phonemic pronunciation (Bright et al., 2002). Further, NART scores were converted and compared to *Wechsler Adult Intelligence Scale (WAIS)* scores for successful premorbid and current IQ comparability of the patient (Pezzuti et al., 2020). Beecroft et al. (1998) used these scores to further understand the cognitive difficulties in patients with pica who have temporal and frontal lobe damage.

Funayama et al. (2017) used the *Mini Mental State Examination- Japanese Version (MMSE-J)* to assess general cognitive functioning in their participants. The MMSE-J is used to assess orientation, attention, memory, working memory, language, and visuo-spatial and written construction (Sakuma et al., 2019).

Funayama et al. (2017) further specifically assessed frontal release signs (frontal lobe) and semantic memory deficits (temporal lobe) to determine a correlation between brain function and pica. Frontal release signs, described as 'primitive reflexes' that are found to be

present in patients with neurological decline and brain injury (Murphy et al., 2015), were assessed by checking 1) grasp reflexes (*Seyffarth's method*), 2) sucking reflexes and 3) utilization behaviours (*The Frontal Behavioural Inventory - Japanese version*). The *Frontal Behavioural Inventory* is an interview with a caregiver and consists of 24 items, however within the study only the question about utilization behaviours was used, being "Does he/she seem to need to touch, feel, examine, or pick-up objects within reach and sight?" (Funayama et al., 2017, p.173).

Further, semantic memory can be described as knowledge accumulated over time and stored in memory (i.e., meaning of words and concepts; Doughty et al., 2008). Funayama et al. (2017) assessed semantic memory deficits by 1) observing the ability to use 10 different objects; 2) administering the three semantic memory questions within *The Informant Questionnaire on Cognitive Decline in the Elderly (IQCOSE)* – Japanese version 3) the use of an interview with a caregiver to assess semantic memory errors in the participants' life.

Neurodevelopmental Disorders. ASD was diagnosed using medical records (Kinnell, 1985; Matson et al., 1999) or questionnaires (Fields et al., 2021). Matson and Bamburg (1999) included a review of medical information by a psychiatrist and Kinnell (1985) noted case records indicated that an ASD diagnosis was made via behavioural observation (i.e., communication difficulties and impairment in gross motor movements). In addition to ICDs-10 classification of ASD in recruited participants, Fields et al. (2021) used the *Social Communication Questionnaire (SCQ)* to ascertain ASD symptoms from four broad categories, namely 1) social engagement, 2) communication, and 3) repetitive and stereotyped behaviour (Schanding et al., 2012). If participants scores were below 11, they would be included as potentially having ASD, regardless of previous ICD-10 diagnosis.

Five of the seven studies that included patients with ID retrieved information through medical records and therefore could not provide the measure used for the diagnosis of ID (Beck et al., 2005; Fields et al., 2021; Josephs et al., 2016; Kinnell, 1985; Matson & Bamburg, 1999). Dumaguing et al. (2003) made use of the *Slosson Intelligence Test*, which assesses IQ. It is important to note that the use of the measure was only mentioned for one of the three cases reviewed in the study (Dumaguing et al., 2003). Lastly, Ashworth et al. (2008) used information from medical records to complete information within the *interRAI ID*, which is a tool that assesses the functioning of an individual with ID. One of the areas for which the tool was used within the study was for clinical purposes (i.e., to ascertain severity of ID).

Psychopathological Conditions. The DSM-IV was used in three included studies for the diagnosis of OCD (Baheretibeb et al., 2008), schizoaffective disorder (Dumaguing et al., 2003) and depression (Bhatia et al., 2009), all of which are mental health disorders commonly found in individuals who present with pica. The manual is used worldwide by practitioners as a guideline for the diagnosis of mental disorders and is to be considered a reliable and standard diagnostic tool (APA, 2013).

A thorough diagnosis was completed by Gundogar et al. (2003) who used both the *Yale-Brown obsessive-compulsive scale (Y-BOCS)* and the *symptom checklist 90-revised (SCL-90-R)* for the assessment of OCD in their patients. The Y-BOCS is used as measure of both the diagnosis of OCD (symptom checklist) and the level of severity (severity scale). However, within the study only the severity scale was used in ascertaining descriptions of the obsessions and compulsions performed (Storch et al., 2010). The SCL-90-R is a self-reported questionnaire, which is used to assess psychopathology. It is comprised of nine subscales of symptoms for specific psychopathology, with obsessive-compulsions being one (Ruis et al., 2014).

Osuji and Onu (2019) also made use of various diagnostic measures within their study. The *International Statistical Classification of Disease (ICD) -10*, a manual used for the diagnosis of various diseases and implemented by the World Health Organization (WHO), was used to diagnose schizophrenia in study participants (World Health Organization [WHO], 1993). Further, the *Mini International Neuropsychiatric Interview (MINI)*, a brief structured interview used to diagnosis a multitude of psychiatric conditions, was used to screen patients for co-morbid psychiatric diagnosis (Sheehan et al., 1998). Lastly, the *Positive and Negative Symptom Scale (PANSS)* was used to assess the various syndromes which fall within schizophrenia (i.e., how they relation to one another and to other disorders; Osuji & Onu, 2019).

Diagnostic Findings

Table 15 outlines the neurological and psychopathological diagnosis and the presentation of pica symptoms. Neurological diagnosis in patients with pica included neurodegenerative diseases, acquired brain injury and stroke. Neurodevelopmental disorders included ASD and ID. Psychopathological diagnosis in patients with pica included OCD, schizophrenia, and depression The most prevalent neurological (neurological diagnosis, neuropsychological profiles, neurodevelopmental disorders) and psychopathological (mental disorders) correlates to pica, presentation of pica symptoms will be outlined below.

Neurological Diagnoses. The most prevalent *neurodegenerative disease* reported in the included articles was Alzheimer's disease (AD). AD was found in five elderly patients (67 to 94 years old) with pica within three included studies [case report (Kanamori et al., 2021); case series (Dumaguing et al., 2003); cross-sectional (Josephs et al., 2016)]. Brain damage within four of the five patients was localized to medial temporal lobe atrophy with three of the patients also presenting with different degrees of frontal lobe atrophy. One out of these four patients also presented with progressive selective atrophy of the hippocampus. The fifth patient presented with generalised cortical and cerebellar atrophy with a small basal ganglia lacunar infarct. Pica symptom onset followed AD diagnosis in four of the patients and preceded it in one patient. Furthermore, pica was found to be more prevalent in patients with late-stage AD (Kanamori et al., 2021)

With regards to other neurodegenerative diseases, frontotemporal dementia (FTD) was found in three patients with pica (Josephs et al., 2016). Two patients presented with the semantic variant (predominantly temporal lobe atrophy, characterised mainly by language difficulties; Snowden, 2023) and one patient presented with the behavioural variant (predominantly frontal lobe atrophy, characterised mainly by personality and behavioural alterations; Snowden, 2023). Brain damage was localized to anterior medial and lateral temporal atrophy in the patients with the semantic variant and bilateral anterior medial temporal lobe atrophy in the patient with the behavioural variant. Pica symptom onset followed FTD diagnosis in all patients.

Multi-infarct dementia was found in one patient who had pica (Dumaguing et al., 2003). The patient presented with gliosis around the areas of which a lobotomy took place, as well as mild to moderate cortical and cerebellar atrophy. Pica symptom onset preceded the diagnosis of multi-infarct dementia.

Acquired brain injury (ABI) in the presence of pica was found in four studies (Beck et al., 2005; Dumaguing et al., 2003; Funayama et al., 2017; Josephs et al., 2016) and included cerebrovascular disease (*n=7*), TBI (*n=2*), brain tumor (*n=1*), encephalitis (*n=1*) and stoke (*n=3*).

Josephs et al. (2016) described one patient who presented with a brain tumour which was classified as a bifrontal glioblastoma multiforme. Pica symptoms onset for the patient started at the same time as the tumour diagnosis.

Additionally, Funayama et al. (2017) described eleven patients with pica. Neuroanatomical analyses demonstrated that most prominent brain region affected within the patients with pica was the temporal gyrus (focus within the left middle temporal gyrus and underlying white matter), $p < 0.01$ (Funayama et al., 2017). Pica symptom onset was not indicated. Funayama et al. (2017) focused their study on investigating *semantic memory deficits* in patients with ABI by comparing a group of patients with pica (*n*=11) to a group of patients with hyperorality (*n*=8). Neuropsychological findings suggested that patients with pica presented with more semantic memory deficits. Specifically, "semantic parapraxis for everyday objects" and "semantic memory errors for tool use", $p < 0.01$ (Funayama et al., 2017, p.175). Furthermore, within the sample group, *transcortical sensory aphasia* and *Wernicke Aphasia* was more evident in patients who demonstrated pica (81.8%), when compared to patients with hyperorality (25%), $p = 0.02$ (Funayama et al., 2017).

Stroke was identified in three patients with pica across the included studies (Beck et al., 2005; Dumaguing et al., 2003; Josephs et al., 2016). For one of the patients, multiple strokes were identified, of which one was a large left parietal infarct with encephalomalacia and the other a lacunar infarct in the basal ganglia (Josephs et al., 2016). As a result of the patient's stroke history, onset of generalized tonic-clonic seizures presented. With regards to the remaining two patients, the specific lesion site was not described (Beck et al., 2005; Dumaguing et al., 2003). For these two patients, we can deduce from the symptomology that one patient had a right hemispheric stroke with symptoms of left hemiparesis and the other a left hemispheric stroke with symptoms of right hemiparesis. In both patients, pica followed the diagnosis of stoke. However, it is important to note that both patients presented with early ID.

Beecroft et al. (1998) investigated a patient (*n*=1) with schizophrenia who presented with frontotemporal atrophy predominantly on the left temporal lobe and right frontal lobe, which could not be accounted for by her schizophrenia. The damage to the regions could be

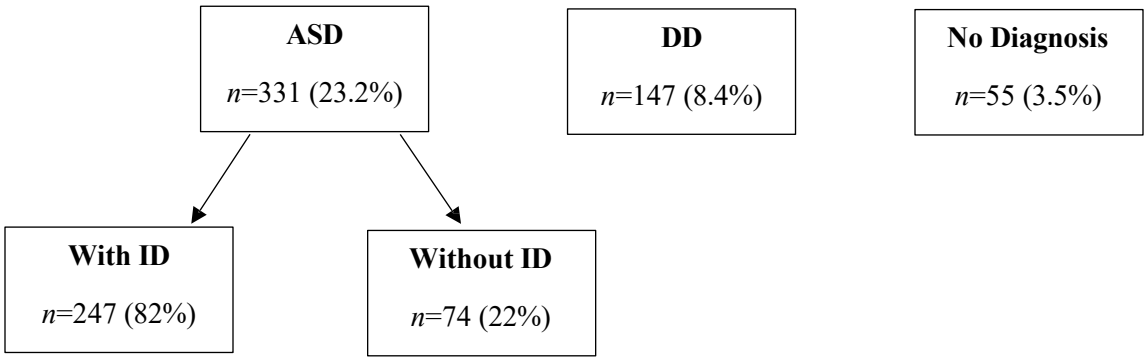
accounted for by the ingestion of inedible objects over the years. The patient presented with a decline in cognitive functioning (IQ=86), when compared to her premorbid state (IQ=106). Her cognitive impairment comprised mainly of difficulties with '*verbal learning, memory, reasoning'* (left temporal damage) and *cognitive switching* (right frontal damage) (Beecroft et al., 1998).

Neurodevelopmental Disorders. In four studies, pica was found to be prevalent in patients with ID with a comorbid diagnosis of ASD (Ashworth et al., 2008; Fields et al., 2020; Kinnel, 1985; Matson & Bamburg, 1999). Ashworth et al. (2008) investigated patients (*n*=1008) with *ID* within an institutionalized setting. The aim of the study was to explore the correlates of an ID diagnosis. Findings indicated that 220 (21.8%) patients with ID presented with pica. In addition, of the 1008 patients diagnosed with ID, only 36 (3.6%) had a comorbid diagnosis of ASD. Further, of the patients with ID and ASD (*n*=36), three (7.3%) presented with pica. Matson and Bamburg's (1999) study included 45 individuals with ID living in institutionalised settings. Findings indicated that 38 of the individuals demonstrated pica behaviours and nine of those individuals had a comorbid diagnosis of ASD.

Fields et al. (2020) study compared children with ASD (*n*=1426), developmental disabilities (DD; *n*=1753) and children without diagnosis (*n*=1578). As indicated in Figure 5, findings highlighted that pica was mostly prevalent in children with ASD (*n*=331; 23.2%), compared to children with DD (n =147; 8.4%) or children without diagnosis (*n*=55; 3.5%). Within the group of children with ASD and pica (*n*=331), pica was more prevalent in children with a comorbid diagnosis of ID (*n*=247; 82%) compared to children without ID (*n*=74; 22%). Lastly, the study done by Kinnell (1985), which focused on pica within patients with ASD and Down Syndrome, indicated that patients with ASD (42 [60%] of those diagnosed) were more likely to present with pica than patients with Down Syndrome (3 [4%] of those diagnosed). Other comorbid disorders which were found to be linked to pica included individuals with ID and stereotypical movement disorder (Matson & Bamburg, 1999). Across all studies, additional factors which demonstrated a significant association with pica amongst those with ID included, increased severity of ID (Ashworth et al., 2008; Kinnell, 1985; Matson & Bamburg, 1999), being male (Ashworth et al., 2008; Fields et al., 2021) and presenting with non-social (expressive and receptive) means of communication (Ashworth et al., 2008; Kinnell, 1985), with the latter being the most prevalent correlate.

Figure 5

Number of Individuals Diagnosed with Pica in Groups Within Fields et al., 2020 Study



Psychopathological Diagnoses. Seven patients who presented predominantly with *OCD* in association with pica, were found across three included studies (Baheretibeb et al., 2008; Gundogar et al., 2003; Stein et al., 1996), all of which were based on case reports. Two patients had comorbid disorders: one patient presented with trichotillomania (obsessive removal of hair which can occur across the body; Melo et al., 2022) and the other patient with panic disorder, agoraphobia, and social phobia (Gundogar et al., 2003, Stein et al., 1996). Most patients described their engagement with pica as being a temptation which could not be resisted often due to intrusive thoughts or the need to perform repetitive behaviour and would often describe feelings of relief after ingesting the material (Baheretibeb et al., 2008; Gundogar et al., 2003; Stein et al., 1996). Two patients described being aware that engagement in pica was not socially acceptable and expressed embarrassment of their behaviour (Baheretibeb et al., 2008; Gundogar et al., 2003). For six of the patients, pica developed after the onset of OCD symptoms (Baheretibeb et al., 2008; Gundogar et al., 2003; Stein et al., 1996).

Schizophrenia was identified in six patients with pica across four studies (Beecroft et al., 1998; Dumaguing et al., 2003; Josephs et al., 2016; Osuji & Onu, 2019). One patient presented with a diagnosis of schizoaffective disorder (Dumaging et al., 2003). The studies ranged from case reports (Beecroft et al., 1998) to cross-sectional studies (Josephs et al., 2016; Osuji & Onu, 2019). Comorbid diagnoses to schizophrenia and pica were identified in three patients: namely ID, psychosis, and stroke (Dumaguing et al., 2003; Josephs et al., 2016; Osuji & Onu, 2019). In three of the patients, pica diagnosis followed schizophrenia

diagnosis. However, due to the nature of Osuji and Onu's (2019) study (large participant size), comorbid disorders and diagnostic timelines were not specified. Osuji and Onu (2019) aimed to identify the most common eating behaviours in patients (*n*=206) with schizophrenia. Controversial to the findings above, the study showed that patients with schizophrenia did not commonly present with inappropriate eating behaviours (*n*=28). Furthermore, of the patients with inappropriate eating behaviours, pica was found to be the least common (*n*=4).

Many of the studies did not specify the patient's reason for their pica behaviour; however, one patient attributed their need for digestion of inedible objects to be due to the 'relief of anxiety' (Beecroft et al., 1998). The study by Beecroft et al. (1998) investigated a patient (*n*=1) with schizophrenia who presented with frontotemporal atrophy predominantly in the left temporal lobe and right frontal lobe, which could not be accounted for by the schizophrenia. The damage to the specified regions could be accounted for by the ingestion of inedible objects over the years. The patient presented with a decline in cognitive functioning (IQ=86), when compared to her premorbid state (IQ=106). Her cognitive impairment comprised mainly of difficulties with '*verbal learning, memory, reasoning'* (left temporal damage) and *cognitive switching* (right frontal damage; Beecroft et al., 1998).

One patient in a case study (Bhatia et al., 2009) presented with *major depressive disorder (MDD)* and pica, with no other comorbidities. As the patient's depressive symptoms (i.e., interrupted sleep, low mood, decline in appetite, sense of hopelessness, lack of interest in activities) increased due to a problematic spousal relationship, the patient started engaging in pica. The patient was aware that the digestion of inedible objects could cause harm and would often attempt to inhibit herself, however by doing so she would increase her anxiety. Only ingestion of the object led to relief. (Bhatia et al., 2009).

Neurological and Psychopathological Overlap. Some studies included patients diagnosed with pica and who presented with both a neurological and psychopathological diagnoses (Beck et al., 2005; Beecroft et al.,1998; Dumaguing et al., 2003; Josephs et al., 2016). These studies presented these patients as case studies. Many of the case studies presented patients who were elderly (65+), who initially were diagnosed with a psychopathological diagnosis (i.e., schizophrenia, schizoaffective disorder) or a neurodevelopmental disorder (i.e., ID), after which they developed pica, then at a later stage developed a neurological condition (i.e., multi-infarct dementia, AD, general tonic-clonic seizures) or presented with cortical atrophy without a diagnosis (i.e., right frontal and left temporal atrophy). Two case studies presented patients who developed pica after a neurological event (i.e., stroke and a frontal lobotomy), however symptoms of pica were only apparent +/- 20 years after the event (Dumaguing et al., 2003). Beck et al. (2005) further presented a patient with a history of depression, cognitive impairment, and stroke; however,

no timeline of the diagnosis was included.

Table 15

Diagnostic Findings

Author	Neurological Diagnosis	Psychopathological Diagnosis	Pica Symptoms
Kanamori et al.	Alzheimer's Disease (atrophy of hippocampus and cognitive impairment) [+/-77] Possible Klűver-Bucy syndrome (oral tendency, prosopagnosia, and placidity)	n/a	Placing toilet paper in mouth and eating pencil shavings initially. Oral tendency of repeatedly licking metal rods. Worsened to eating weeds and dishwashing sponge. [+/-79]
Beecroft et al.	Frontotemporal atrophy most marked on the left in the temporal lobe and on the right in the frontal lobe [75]	Schizophrenia (without positive symptoms) [32]	Compulsion to eat vitamin C tablets for anxiety relief. Emergency laparotomy due to lose change in stomach. [43]
Bhatia et al.	n/a	Depression [33]	As her depressive symptoms became worse, she developed a desire to eat chalk. Following arguments with her husband, she developed thoughts of eating chalk and were only relieved once she ate it [34]
Beck et al.	Stroke with left hemiparesis. Possible second stroke. Mild mental retardation.	Depressive Disorder.	Urination and defecation oneself. Frequent ingestion of own faeces.
Baheretibeb et al.	n/a	Obsessive-Compulsive Disorder (moderately severe). [17]	Recurrent intrusive images and thoughts of mud and of eating mud. Feelings of anxiousness that were relieved when consuming mud. Uncontrollable need to return home to eat mud from wall. Abdominal distention and constipation and cramping and pain. [>2].
Dumaguing et al.	Stroke– developed right hemiparesis and memory loss [59]. Dementia praecox [19] and Multi-Infarct Dementia [63]. Alzheimer's-type Dementia [88]	Schizophrenia, Schizoaffective Disorder [possibly since young adulthood], Paranoid Schizophrenia	Ingestion of foreign objects [76]. Having ritualistic behaviour which included eating faeces, fingernails, and hair to preserve his parts. Became obsessed with drinking urine [40]. Pica behaviour included swallowing cigarette butts, faeces, and garbage [46].

	Developmental delay (mild- severe)		
Gundogar et al.	n/a	Obsessive-Compulsive Disorder	Eating cigarettes was an urge she felt while smoking which she couldn't resist, even though she felt regretful afterwards. Hair-pulling, hair-eating, and paint licking. Could not resist temptation to eat hair.
Stein et al.	n/a	Obsessive-Compulsive Disorder, Panic Disorder, Agoraphobia, and social phobia, depression.	Eating of sand which was described as a repetitive behaviour that she felt compelled to carry out. Urge to eat certain sorts of dry dog faeces followed by purging (felt compelled to do). Eating 15 sticks of chalk a day which led to gratification from tension. Eating of newspaper to decrease sense of tension/ stress.
Josephs et al.	Frontotemporal Dementia, Alzheimer's, General Tonic-Conic Seizures following stoke, Frontal Lobe Tumour Developmental Delay	Schizoaffective Disorder, Steroid Psychosis	Varying descriptions of pica behaviour: "did not like eating faeces but is unable to discontinue eating it"; "she was laying eggs"; "tired of living this way" and hence ate faeces to commit suicide (E. coli bacteria in faeces would kill him).
Matson et al.	Intellectual Disability, Autism Spectrum Disorder,	Stereotypic Movement Disorder	Main reason for engaging in pica were for predominantly non-social reasons (automatic reinforcement). Other reasons include to obtain tangible objects or to get staff attention.
Osuji et al.	n/a	Schizophrenia	-
Ashworth et al.	Intellectual Disability	n/a	-
Funayama et al.	Acquired Brain Injury	n/a	-
Fields et al.	Autism Spectrum Disorder, Developmental Disabilities	n/a	-
Kinnell	Autism Spectrum Disorder, Down Syndrome, All severely handicapped	n/a	-

Note. n/a indicated that the patient has not been diagnosed within this category. (-) indicated that a description of pica symptoms was not included in the journal article. Information in [brackets] includes age of onset.

Pharmaceutical Treatment Results

Table 16 outlines the included articles which explored the treatment of pica within patients. The pharmaceutical treatment results will be outlined below. The information extracted within this section aims to aid the discussion of whether pica is associated with neurological and psychopathological correlates by unpacking which groups of medications are predominantly used in treating neurotransmitter dysregulation in patients with specific neurological and psychopathological diagnosis, which in turn stopped pica behaviour.

Successful. Pharmaceutical treatments which were effective in stopping pica behaviours includes medication within the following groups: selective serotonin reuptake inhibitors (SSRI's), serotonin antagonists and reuptake inhibitors (SARI's), tricyclic antidepressants (TCA), benzodiazepine and anti-psychotic medication.

SSRIs. Five studies demonstrated that pica can be resolved with the use of SSRI treatment. SSRIs are generally used to treat varying psychiatric conditions (Chu & Wadhwa, 2023). The mechanism includes the inhibition of serotonin reuptake, which in turn increases serotonin levels (5-hydroxytryptamine) within the brain. Importantly, SSRIs have no impact on other neurotransmitters (Chu & Wadhwa, 2023). *Sertraline* was used in three patients, in varying dosages (25mg – 200mg), whom had pica and either MDD (Beck et al., 2005), OCD (Gundogar et al., 2003) or OCD and social phobia (Stein et al., 1996). In all three cases, both pica and the comorbid disorder resolved after 12 weeks. *Citalopram*, in varying dosages (20mg-80mg) was used to treat three patients with pica, two of whom had OCD and one who had MDD and anxiety. Both pica and comorbid disorders improved within 4 to 12 weeks. *Fluoxetine* (40mg) was used in two patients who had pica and OCD, after which both disorders resolved after 4 weeks (Gundogar et al., 2003).

SARIs. Trazodone is a SARI, used to treat MDD and to treat symptoms within patients with AD and FDD (López-Pousa et al., 2008). The mechanism of trazodone is two-fold: it acts as an inhibitor of serotonin transportation (SERT) and as an antagonist of serotonin type 2 (5-hydroxytryptamine), adrenergic and histamine receptors (Fagiolini et al., 2012). One study found that SARI (trazodone: 50mg) in combination with SSRI (fluvoxamine:75mg) were effective in treating pica in a patient with AD (Kanamori et al., 2021).

TCA. Clomipramine is a TCA, with the mechanism of increasing serotonin and norepinephrine within the brain (Hollander et al., 2000). Clomipramine (75mg) was found to be an effective treatment of pica in one patient with OCD, after 3 months (Baheretibeb et al.,

2008). However, Stein et al. (1996) found clomipramine (75mg – 300mg) to be ineffective in treating pica in two patients with OCD. The treatment aided in treating OCD symptoms, however pica symptoms remained.

Benzodiazepine. Clonazepam is a benzodiazepine, with the mechanism of binding GABA (y-Aminobutyric acid) to various GABA receptors (Wafford, 2005). Bhatia and Gupta (2009) found that the combination of clonazepam, at 0.25mg, with escitalopram (SSRI) was effective in treating pica after 3 weeks, in a patient with depression.

Antipsychotic Medication. Haloperidol is a first generation (typical) antipsychotic, with the mechanism of acting as an antagonist for the dopamine receptor (D2; Zhao and Li, 2009). Josephs et al. (2016) found haloperidol (1-3mg) effective in treating four patients with pica (coprophagia: consumption of faeces), however the treatment did not work for all patients. Furthermore, pimozide, which is a conventional antipsychotic, has the mechanism of inhibiting dopamine receptors (D2; Kasanami et al., 2022). Kinnell (1985) found that pimozide (12mg) aided in reducing pica behaviour (acuphagia: consumption of sharp objects) in a child (10-year-old) with ASD, however it did not remove it completely.

Unsuccessful. Across four studies (Dumaguing et al., 2003; Josephs et al., 2016; Kanamori et al., 2021; Stein et al., 1996), certain pharmaceutical treatments for pica were shown to be ineffective for some patients, while effective in others. Such medications included anti-psychotics (haloperidol), benzodiazepines (clonazepam), TCA (clomipramine) and SARI (trazodone; Dumaguing et al., 2003; Stein et al., 1996). Other medications which were ineffective were used in patients who displayed pica later in life and who were on the medications before pica began (Dumaguing et al., 2003). These included medications for the treatment of AD (Rivastigmine and Memantine), benzodiazepines (lorazepam), antiepileptic (valproic acid), antipsychotic (quetiapine, Thioridazine, thiothixene, fluphenazine, molindone), anticonvulsant (Carbamazepine) and antidepressants (mirtazapine; Dumaguing et al., 2003; Josephs et al., 2016; Kanamori et al., 2021).

Table 16
Treatment and Findings

Author	Diagnosis in Addition to Pica	Treatment	Effectiveness in Treating Pica
Kanamori et al.	Alzheimer's Disease	Memantine 20mg + olanzapine 1.25mg + perospirone 4mg	No
		Trazodone 50mg + fluvoxamine 75mg	Yes
Beecroft et al.	Schizophrenia	Cognitive-behavioural Approach	Yes (partially)
Bhatia et al.	Depression	Escitalopram 10mg + clonazepam 0.25mg + supportive therapy	Yes
Beck et al.	Stroke + Mild mental retardation + Depression	Sertraline 25mg	Yes
Baheretibeb et al.	OCD	Clomipramine 75mg + clinical interview	Yes
Dumaguing et al.	P1: Stroke + Developmental delay + schizoaffective disorder P2: Dementia praecox and Multi-Infarct Dementia + mild developmental delay P3: Alzheimer's-type Dementia +paranoid schizophrenia	P1: thioridazine + haloperidol, carbamazepine + benzodiazepines (clonazepam and lorazepam) + behavioural interventions. P2: Thioridazine 200 - 300mg/day + benzodiazepines + Behavioural interventions. P3: chlorpromazine + thioridazine, haloperidol + thiothixene, fluphenazine + molindone + Behavioural interventions	No
Gundogar et al.	OCD	P1: Fluoxetine 40mg P2: Fluoxetine 40mg P3: Sertraline 150mg	Yes
Stein et al.	OCD	P1: sertraline 200mg P2: citalopram 80mg P3: clomipramine 75mg P4: clomipramine 300mg (switched to citalopram 60mg) P5: citalopram 20mg	P1: Yes P 2: Yes P3: No P4: No (Yes) Pt 5: Yes
Josephs et al.	Alzheimer's Disease, Frontotemporal Dementia, seizures, developmental delay, schizoaffective disorder	Lorazepam, Trazodone, mirtazapine, valproic acid, quetiapine, and haloperidol	Haloperidol (Yes) Other medication (No)
Kinnell	ASD	Pimozide 12mg	Yes (less frequent)

Discussion

The aim of the SR was to investigate the current neurological and psychopathological correlates of pica. Pica, being described as the consumption of non-nutritive substance (APA, 2022), has been prevalent within vulnerable population groups including children (Murray et al., 2018), pregnant women (Sanjari et al., 2023), institutionalised individuals (Papini et al., 2023) as well as individuals who are diagnosed with neurological (Funayama et al., 2017; Kanamori et al., 2021) or psychopathological conditions (Baheretibeb et al., 2008; Osuji & Onu, 2019). Even though descriptions of pica have been dated since 400 BCE (Ali, 2001), challenges with understanding the mechanisms and aetiologies are ongoing and has led to difficulties in establishing adequate treatment plans. This, in turn, has led to many undiagnosed cases and unsuccessful treatment of pica which has contributed to complications such as intestinal blockage, infections, poisoning and even death (Ali, 2001; Byard, 2014; Williams & McAdams, 2012).

With the array of aetiologies associated with pica, the dominant one being a nutritional deficiency, specifically in iron and zinc, identifying and understanding the less researched correlates and their relation to one another may aid in unpacking other causal links to the development of pica. Studies have identified some psychopathological disorders such as OCD and schizophrenia as being comorbid disorders with pica, however limited research has aimed to identify whether the mechanism in the development of pica lies within these diagnoses, in other words, whether these are correlates/comorbid disorders or causal. Similarly, limited research has aimed to identify, systematically, neurological (and neurodevelopmental) conditions which are correlated with pica or whether the neurological sequelae as a result of these conditions are linked to a mechanism within the development of pica. Further, there has been a dearth of research done on the links between the presentation of dual psychopathological and neurological symptoms/disorders in patients presenting with pica, hence the contribution of the current study.

Against this background, the discussion will unpack 1) factors which could affect interpretation of results; 2) what current research has found to be the most prevalent 2.1) neurological conditions, brain regions, neuropsychological presentations and neurodevelopmental disorders related to pica; 2.2) psychopathological conditions and patient presentation of conditions; 3) dual neurological and psychopathological presentations, and 4) successful pharmacological treatments, including which neurotransmitter links are correlated with the treatment of pica. Lastly, limitations and recommendations of the current evidence

and the review process will be explored as well as the implications of the findings on identifying and treating pica.

Factors to Consider when Considering the SR Design and Interpreting the Results of the Study Designs.

Methodological Quality

This SR included 15 articles compared to other recent SR's ([n=79]; Leung & Hon, 2019; [n=46]; Williams et al., 2022), however these SR's were focused on a general overview of pica. Due to the few articles included within this SR, the methodological quality of the articles is important. Within this SR, two articles demonstrated a high risk of poor methodological quality (case reports [0/5], case series [1/3], case control [1/3] and cross-sectional [0/4] study designs). These articles evidenced poor internal validity (demonstrating bias) and reliability by obtaining methodological quality scores of 44.5% (Dumaguing et al., 2003) and 33.3% (Finnell, 1985). These articles were included within the SR due to the limited number of articles which were not case report or case series designs. Therefore, interpretation of these articles within the SR needs to be reviewed with caution.

Eight of the 15 articles included within the SR were case reports and case series, accounting for more than half of the included articles. Due to the limited research within the field of diagnosed conditions and its association with pica, these articles have been included within this SR. Further, the quantitative method (descriptions) linked to case reports and series provide insight into the patient's history and experience of the diagnosis, which was valuable within this SR (Quintão et al., 2020). However, case studies and case series should be interpreted with caution because they lend to researcher bias (i.e., the researcher's close involvement with identifying cases and data collection) and the lack of generalizability, both which influences validity and reliability of results (Leung, 2015).

Despite the evidence of this SR extracted, following a systematic reviewing of literature, the overall findings will be discussed below.

Nutritional Deficiency

Nutritional deficiency, specifically iron and zinc, has been established as the most common correlate to a pica diagnosis, even though the causal links are unknown (Ganesan & Vasauskas, 2023; Miao et al., 2015; Young, 2015). Therefore, including studies which includes patients with nutritional deficiencies may confound the consideration of correlations between neurological or psychopathological conditions and possible pica aetiology. To eliminate this possible confounder, all studies included only included patients without nutritional deficiencies.

Pica Diagnostic Tool

Across the articles included many (Beck et al., 2005; Beecroft et al., 1998; Funayama et al., 2017; Josephs et al., 2016; Kanamori et al., 2021; Kinnell, 1985; Stein et al., 1996) did not provide a clear description of the measure used and others (Ashworth et al., 2008; Fields et al., 2021; Osuji & Onu, 2019) made use of self-report questionnaires to identify patients with pica symptoms. A few studies (Baheretibeb et al., 2008; Bhatia & Gupta, 2009; Dumaguing et al., 2003; Gundagar et al., 2003; Matson & Bamburg, 1999) made use of the DSM-IV to inform the diagnosis of pica, often by a trained professional. The latter approach, using DSM criteria, is the gold standard approach. Such differences in diagnostic measures are consistent with the varied definitions for pica included in the literature, with some definitions including starch and ice as non-nutrient substances and others included individuals who engage in pica for cultural purposes (Hartmann et al., 2012).

This poses as a confounding factor when interpreting the results as a standard definition and measurement tool was not used across all included articles, therefore difficulties arise in confidently interpreting all pica diagnoses as definite. To minimize the effect of these varied definitions, the SR only included articles which followed the description of pica provided by the DSM-5-TR, which excludes patients who engage in eating ice or starch and who engage in pica for cultural or traditional purposes (APA, 2022). This allows for a more standard definition to apply to the articles included within the SR. Even though measures have been taken to mitigate the effects of the varied definitions of pica, the large number of articles included which did not clearly provide a standard measure for pica (n=7) could affect the interpretation of results.

Pica as a Predictor of Neurological Changes

Even though minimal research has been conducted regarding whether neurological conditions may result in, or produce vulnerabilities which may encourage, pica, even fewer studies have explored whether the reverse could be true. Lead consumption has been documented as a non-nutritive substance ingested in some patients diagnosed with pica. Studies have identified that lead consumption could result in progressive encephalopathy and oedema possibly due to lead's ability to 'act as' calcium therefore affecting the blood-brain barrier (Maslinkski & Loeb, 2004; Sabourand et al., 2009). To mitigate whether pica could have resulted in some of the neurological or neuropsychological findings, most of the studies included identified pica diagnosis following the neurological condition not preceding it.

Neurological and Psychopathological Correlates of Pica

A summary of the neurological and psychopathological correlates of pica can be found in Table 17 below.

Neurological Correlates of Pica

Various neurological conditions, most prominently, neurodegenerative disease such as AD (Kanamori et al., 2021; Dumaguing et al., 2003; Josephs et al., 2016), FTD (Josephs et al., 2016), multi-infarct dementia (Dumaguing et al., 2003), ABI (Funayama et al., 2017; Josephs et al., 2016) and stroke (Beck et al., 2005; Dumaguing et al., 2003; Josephs et al., 2016), were found to be most prevalent in patients with pica. The diagnosis of pica followed the diagnosis of the neurological condition, supporting the idea that pica could be a consequence of the neurological diagnosis.

Neuropathology. Importantly, the neuroanatomical region of damage across the above neurological conditions were found to be similar, supporting the conjecture that damage to certain brain regions is more likely to be correlated with the development of pica than others. Therefore, across the various neurological conditions, damage to the frontal and temporal cortex and hypothalamus were often found to be correlated with pica (Funayama et al., 2017; Josephs et al., 2016; Kanamori et al., 2021)

Although research regarding pica's correlation with neurological conditions and neuroanatomical regions has been limited, studies have documented an association between common eating disorders such as anorexia nervosa and bulimia nervosa and its correlation with structures close to the limbic system such as frontal and temporal regions and the hypothalamus (Uher & Treasure, 2005; Liu et al., 2004; Trummer et al., 2002). Frontal regions provide higher order functions (i.e., decision-making and inhibition) and motivational processes that promotes behaviour (Siddiqui et al., 2008). Dysregulation within these structures could contribute to eating disorders through difficulties with decision-making (restricting food intake), inability to control impulses (binge eating) and inadequate motivational processes (motivation to relief anxiety by restricting food intake) regarding food behaviours (Siddiqui et al., 2008). Dysfunction within the temporal cortex, which plays an essential role in emotional regulation, has been shown to be evidenced in high levels of anxiety (increase in activation of temporal lobes), which is commonly found in patients with eating disorders (Frank, 2013). This level of emotional dysregulation contributes to body image difficulties which is a commonality within individuals suffering from anorexia nervosa and bulimia nervosa (Downing et al., 2001). The hypothalamus has been found to contribute to eating disorders due to its involvement in regulating the consumption of food and maintaining energy homeostasis through metabolising, which is modulated through neuronal networks (Tolle et al., 2021). This postulates a link between eating disorders and frontal-

temporal and hypothalamic brain regions.

Other research on FTD and AD and changes in eating behaviours (Ikeda et al., 2002; Aiello et al., 2016), support this link too. When compared, patients with FTD (semantic and behavioural variant), were more likely to exhibit changes in eating behaviours when compared to patients with AD (Ikeda et al., 2002). Patients with FTD (semantic and behavioural variant) often display changes in eating behaviours which includes changes in eating habits, however patients with semantic variant also display oral tendencies (Ikeda et al., 2002).The association between these eating behaviours and FTD was once again found to be due to the involvement in the frontotemporal cortex (orbitofrontal and temporal pole) and hypothalamus (Ikeda et al., 2002; Aiello et al., 2016).

In addition, research regarding Klűver-Bucy syndrome (KBS), which results following reduction of bilateral temporal lobes due to epilepsy, indicates that a prominent symptom which often presents include the oral examination of objects. Again, KBS has been found to be linked to damage within the "white matter tracts in the temporal lobe and hippocampus" (Boronat et al., 2013, p.1392; Kim et al., 2011). These findings further point to a possible association between structures surrounding the limbic system and the development of oral-object fixation (Boronat et al., 2013).

Further, as indicated by Funayama et al. (2019), individuals who experienced an ABI within the middle temporal gyrus, later presented with pica behaviours. Damage to the above-mentioned neuroanatomical region, resulted in semantic memory deficits within these individuals. Semantic memory deficits often follow damage to frontotemporal white matter connections (arcuate and longitudinal fasciculus; Robinson et al., 2012; Vignando et al., 2020). Damage to the frontotemporal white matter tracts has been found to evidence a significant relationship with alterations in eating habits (Vignando et al., 2020). These findings further support the correlation between frontotemporal regions and pica.

Although the neuroanatomical regions mentioned above were the most frequently reported, damage to other brain regions were found within patients with pica, however these only occurred within two patients. Specific brain regions included generalised cortical atrophy as well as cerebellar atrophy with a small basal ganglia lacunar infarct (Dumaguing et al., 2003; Josephs et al., 2016).

Neuropsychological Correlates of Pica. Given that frontotemporal regions have been found to be the most prominent neuroanatomical region associated with pica, the related neuropsychological outcomes were also investigated. Two articles included reported on the neuropsychological profiles of individuals with pica (Beecroft et al., 1998; Funayama et al., 2017). In one article (Funayama et al., 2017), *semantic memory deficits* and *aphasia* (transcortical sensory and Wernicke's) were reported and in the other (Beecroft et al., 1998)

cognitive difficulties following left temporal (verbal learning, memory, and reasoning) and right frontal (cognitive switching) damage were reported.

Semantic Memory Deficits. Studies have found that the worse patients with FTD and AD perform on semantic tasks, the more likely they would be to exhibit changes in eating behaviours (i.e., habits and preferred foods; Vignando et al., 2020). These findings point to a correlation between semantic memory deficits and management of eating behaviours (Thompson et al., 2016). It further suggests that a decline in knowledge regarding food could lead to eating alterations, which could impact acceptable food related behaviours (Vignando et al., 2020). The types of semantic difficulties strongly related to eating alterations included naming as well as matching words and pictures, for both food and non-food items (Vignando et al., 2020). These findings support the notion that the semantic memory system contributes to maintaining eating habits.

Aphasia. Aphasia can be defined as difficulties in expressive (comprehension) or receptive (comprehension) communication (Zhang & Hinzen, 2022). Even though associations between aphasia and pica have been found within this SR (Funayama et al., 2017), research outside of this have found no correlations between changes in eating behaviours and TSA nor Wernicke's aphasia. As noted above, due to the limited number of articles included within the SR, data extracted should be done with caution. Therefore, even though an association was found between TCA and Wernicke's aphasia, it was only reported in one included article (Funayama et al., 2017) and further evidence does not provide support for this association.

Neurodevelopmental Correlates of Pica. Severe and profound ID (Ashworth et al., 2008) and ASD (Fields et al., 2021; Kinnell, 1985; Matson & Bamburg, 1999), were the most common NDD associated with pica in this SR. What makes these correlates complicated is that they are rarely found in isolation, as they are often accompanied by comorbid disorders such as schizophrenia (Dumaguing et al.., 2003; Josephs et al., 2016), depression (Beck et al., 2005) or a combination of ASD and ID (Fields et al., 2021; Kinnell, 1985; Matson & Bamburg 1999), all of which are also found to be correlates of pica independently.

In addition, individuals with ID could present with an array of neuroanatomical changes/damage resulting from TBI or congenital brain conditions, which accounts for their development of ID (Johns & Adnams, 2016). Therefore, isolating brain regions of individuals with ID is not feasible. In terms of neuroanatomical connectivity and ASD, studies mainly indicate an increase in activity in temporal-occipital regions and underactivity in frontal regions (Keown et al., 2013), again, possibly supporting the idea that temporal and frontal regions may be involved in the development of pica.

Pica amongst individuals with ID were mainly found in those living in

institutionalized settings (Ashworth et al., 2009). A precursor to pica behaviour within this population may be the severity of the conditions presented within institutionalized individualised, often including severe developmental delay in addition to various comorbid diagnoses (Ashworth et al., 2008; Fields et al., 2020; Kinnel, 1985; Matson & Bamburg, 1999). These individuals are more likely to be functioning at a younger age range. This could lead to a higher likelihood of oral fixated behaviours because of sensory processing, which is often found to be acceptable within children younger than two (Kesavelu & Anandapandian, 2021) or within children demonstrating ASD symptoms (Bryson et al., 2007) to relieve anxiety.

Psychopathological Correlates of Pica. The most prominent psychopathological correlates of pica were found to be OCD (Baheretibeb et al., 2008; Gundogar et al., 2003; Stein et al., 1996), schizophrenia (Beecroft et al., 1998; Dumaguing et al., 2003; Josephs et al., 2016; Osuji & Onu 2019) and depression (Beck et al., 2005; Bhatia et al., 2009; Stein et al., 1996).

OCD. When assessing the psychological symptoms of OCD, studies have found the basis to be anxiety, which is formed through obsessive consistent intrusive thoughts (Stein et al., 2019). It is put forward that patients then feel compelled to perform repetitive behaviours to alleviate the feeling of anxiety (Stein et al., 2019). Studies included within the SR indicated a similar pattern of anxiety due to intrusive thoughts, which seemed to be alleviated once the patient engages in pica as a form of such compulsion (Baheretibeb et al., 2008; Gundogar et al., 2003; Stein et al., 1996).

Regarding the pathophysiological considerations, studies show that the neuroanatomical structures involved in OCD are cortical structures such as orbitofrontal regions (reinforcement and learning (rewards; Kringelback, 2005) and anterior cingulate cortex (decision making and negative emotions [anxiety]; Huey et al., 2008) as well as subcortical structures such as the basal ganglia (emotional processing; Frank et al., 2001) and

the thalamus (relay pathway to other brain regions; Friedlander et al., 2004). As previously mentioned, structures involving the frontal cortex (orbitofrontal) as well as structures involving the limbic system (basal ganglia and thalamus) have been found to be correlated to changes in eating behaviours (Ikeda et al., 2002; Aiello et al., 2016), therefore indicating a possible link between the underlying mechanism of OCD and pica.

Schizophrenia. The psychological symptoms of patients with schizophrenia are reported as positive (hallucinations and delusions; Fletcher & Frith, 2008) and negative ("blunted affect, alogia (limited speech), avolition (decreased motivation), asociality (decreased need to engage socially), and anhedonia (inability to feel pleasant emotions"; Correll & Schooler., 2020, p. 519). Unfortunately, most of the studies included in the SR with correlations of schizophrenia to pica (Dumaguing et al., 2003; Josephs et al., 2016; Osuji & Onu, 2019), did not discuss the possible psychological reasoning for the patients' need to eat inedible objects, with just one study pointing towards alleviation of anxiety (Beecroft et al., 1998). However, a recent study which was published following the literature search for this SR, indicated that schizophrenia results in pica behaviour because of delusional beliefs (Vanderburg et al., 2024). The delusional beliefs reported included a belief that the consumption of non-nutritive substances would encourage digestion, possibly providing health benefits (Vanderburg et al., 2024). This association suggests that pica could be a result of positive schizophrenic symptoms, as these beliefs motivated the individual to partake in pica behaviours. Not all the articles included within the SR reported noteworthy associations between schizophrenia and pica, with pica being found to be the least common eating disorder amongst patients with schizophrenia (Osuji & Onu, 2019).

Studies have also shown that the neuroanatomical structures involved in long-standing schizophrenia include cortical regions such as the frontal and temporal cortex as well as subcortical regions such as the hippocampus, basal ganglia, and amygdala, all which indicated a reduction in size (Danielyan & Nasrallah, 2009; Valakoulis et al., 2006). As indicated in the previous section on neurological correlates, similar regions (i.e., frontal, temporal, hippocampus) were found to be associated with pica in studies on neurological correlates included in the SR (Josephs et al., 2016; Funayama et al., 2017; Kanamori et al., 2021).

Depression. Psychological symptoms of depression include but are not limited to, interrupted sleep, low mood, decline in appetite, sense of hopelessness, lack of interest in activities (Ostinelli et al., 2021). Three studies within the SR (Beck et al., 2005; Bhatia & Gupta, 2009; Stein et al., 1996) presented three patients with depression, one of which had a

comorbid diagnosis of with anxiety, which is found to be commonly associated (Kalin, 2020). The relation of these disorders to pica were described as being a relief of anxiety (Bhatia & Gupta, 2009) and tension build up (Stein et al., 1996).

Further, studies have demonstrated that the neuroanatomical structural changes associated with depression include reduced volume in cortical structures such as the frontal and orbital-frontal regions as well as subcortical structures and circuits within the limbic system (Miguel & Rajkowska, 2002; Rajmohan & Mohandas, 2007). Again, this corresponds with correlated regions identified in patients with pica (Josephs et al., 2016; Funayama et al., 2017; Kanamori et al., 2021) as well as patients with FTD who present with changes in eating behaviours (Ikeda et al., 2002; Aiello et al., 2016).

All the psychopathological conditions described vary in symptomology, however what was found to be common across these studies were certain brain regions which were implicated across the neuropathology of these disorders, namely frontal and temporal structures as well as structures within the limbic system. In addition, even though a lack of reporting with regards to the reason for the engagement of pica behaviour within patients with schizophrenia was limited, a common thread exists between the reason for engagement amongst patients with OCD and depression, with the relief of anxiety being the central reason.

Dual Diagnoses

Various studies within the SR (Beck et al., 2005; Beecroft et al.,1998; Dumaguing et al., 2003; Josephs et al., 2016) included patients with both neurological (multi-infarct dementia, AD, general tonic-clonic seizures), including neurodevelopmental conditions (ID), and psychopathological (schizophrenia) diagnoses. Most of the studies indicated that pica was usually diagnosed following the psychopathological condition (Beecroft et al.,1998; Josephs et al., 2016), however one indicated onset of pica some years after the neurological condition (Dumaguing et al., 2003). It is, therefore, important to establish understanding of cases in which patients present with pica and dual diagnoses with caution when aiming to pinpoint causal or correlated contributions to the development of pica. Nevertheless, dual diagnoses are apparent amongst individuals with pica therefore making it difficult to tease apart how certain conditions are correlated to the feeding disorder.

Table 17
Summary of the Neurological and Psychopathological Correlates of Pica

	Neurological Correlates					Psychopathological correlates
Author	Neurological diagnosis	Brain regions	Neuropsychological profile	Neurodevelopmental disorders	Neurotransmitter dysregulation treated	Psychopathological diagnosis
Kinnell	n/a	n/a	n/a	ID, ASD, Down syndrome	Dopamine*	
Stein et al.	n/a	n/a	n/a	n/a	Serotonin, serotonin & norepinephrine*	OCD, depression, anxiety
Beecroft et al.	n/a	Frontotemporal atrophy (L temporal/R frontal)	Difficulties with verbal learning, memory, reasoning, cognitive switching	n/a	n/a	Schizophrenia
Matson & Bamburg	n/a	n/a	n/a	ID, ASD	n/a	n/a
Dumaguing et al.	AD, multi-infarct dementia, stroke	Cortical and cerebellar atrophy. Basal ganglia.	n/a	ID	Dopamine*, GABA*	Schizophrenia, Schizoaffective disorder
Gundogar et al.	n/a	n/a	n/a	n/a	Serotonin	OCD, trichotillomania, panic disorder, agoraphobia
Beck & Frohberg	Stroke	n/a	n/a	ID	Serotonin	MDD
Ashworth et al.	n/a	n/a	n/a	ID, ASD	n/a	n/a
Baheretibeb et al.	n/a	n/a	n/a	n/a	Serotonin & norepinephrine	OCD

Bhatia & Gupta	n/a	n/a	n/a	n/a	Serotonin & GABA	Depression
Josephs et al.	AD, FTD, ABI, Stroke	Medial temporal and frontal lobe atrophy, bifrontal regions, L parietal, basal ganglia	n/a	n/a	Dopamine*	Schizoaffective disorder
Funayama et al.	ABI	L middle temporal gyrus and underlining white matter	Semantic memory deficits, TCA and Wernicke aphasia	n/a	n/a	n/a
Osuji & Onu	n/a	n/a	n/a	n/a	n/a	Schizophrenia
Fields et al.	n/a	n/a	n/a	ID, ASD	n/a	n/a
Kanamori et al.	AD	Hippocampus	n/a	n/a	Serotonin	n/a

Note. n/a indicates that the article did not include information in relation to this category; * indicates that the treatment was either not successful for all patients or it only reduced pica behaviour (did not completely treat it). Most common neurological conditions are highlighted in purple. Most common brain region is highlighted in blue. Most associated neurodevelopmental disorders are highlighted in red. Most associated neurotransmitter (treatment led to termination of pica) is highlighted in green. Most associated psychopathological correlates are highlighted in orange.

Pharmaceutical Treatment and Neurotransmitters

Many articles included in the SR demonstrated that certain pharmaceutical treatments were successful in treating pica. The most common successful treatments reported were SSRIs and SARIs, both of which involves serotonin whether it be in an inhibiting or antagonistic manner (Beck et al, 2002; Gundogar et al., 2003; Stein et al., 1996). All articles demonstrated that the use of SSRIs was successful in treating both pica and the comorbid psychopathological conditions namely OCD, depression, or social phobia. One study found the combination of SSRIs and Benzodiazepine (binding GABA) to be successful in treating pica in a patient with depression. Furthermore, SARIs were successful in treating pica in a patient with AD (Kanamori et al., 2021). Other treatments included TCA (increasing serotonin and norepinephrine) and antipsychotic medication (antagonist for dopamine receptor), however treatment success with regards to pica varied amongst patients (Josephs et al., 2016; Stein et al., 1996; Kinnel, 1985).

These findings indicate three possible correlations: firstly, that pica does not seem to be an independent diagnosis from psychopathological conditions, as treatment of the conditions results in the treatment of pica as well; secondly, that pica can possibly be treated in isolation of a comorbid condition (AD); and thirdly, that there could be a relationship between pica and disruptions within the neurotransmitter system specifically in relation to serotonin.

Limitations of Included Studies

As indicated in Table 18, across the articles included, small sample size, sample selection, cross-sectional design, and non-standardised tools use for diagnostic and outcome measures were identified as key limitations in those studies. The above limitations will be discussed in detail below. Several included studies did not provide clear limitations to their studies (Beck et al., 2005; Beecroft et al., 1998; Bhatia & Gupta, 2009; Gundogar et al., 2003; Josephs et al., 2016; Kinnel, 1985; Matson & Bamburg, 1999; Stein et al., 1996), mainly due to a large number of case study and case series study designs, as well as a lack of comprehensive reporting.

Sample Size

Small sample sizes were identified explicitly as a limitation within two studies (Baheretibeb et al., 2008; Funayama et al, 2017), however many of the studies included presented case reports or series (Beck et al., 2005; Beecroft et al., 1998; Bhatia & Gupta, 2009; Dumaguing et al., 2003; Gundogar et al., 2003; Kanamori et al, 2021). Case reports

and case series have the risk of not being generalizable and could lead to poor validity and reliability, therefore interpretation of these results cannot be used for the general population. Further, small samples size within a case control study (Funayama et al., 2017) poses the risk of not being able to present a true effect and should statistical significance be achieved, it may be exaggerated (Button et al., 2013).

Sample Selection

Sample selection was identified as a limitation due to the selection of participants from institutionalized settings or hospitals (Osuji & Onu, 2019). The selection of participants from hospitalized settings results in a lack of generalization to the general population. This means that findings obtained across these studies can only be applied to patients residing in similar institutions.

Cross-Sectional Design

One study highlighted limitation as the data being cross-sectional in nature (Ashworth et al. 2008). It is important to note, that several other studies included were also cross-sectional in design (Josephs et al., 2016; Matson & Bamburg, 1999; Osuji & Onu, 2019). The negative consequence of this design is that it captures information within one timepoint and therefore behaviour is not measured or reflected over time (Wang & Cheng, 2020). Even though cross-sectional studies are used to determine prevalence of an outcome, it is not typically used to determine cause and effect (Wang & Cheng, 2020).

Tools used for Diagnostic and Outcome Measures

Some studies identified the tools used to diagnose and define pica were not standardized (Fields, et al., 2021; Osuji & Onu, 2019). For example, Fields et al. (2021), identified that they used semi-structured caregiver reported interview to ascertain pica behaviours and Osuji and Onu (2019) made use of self-reported questionnaires, instead of a more standardized tool (DSM). The effect of using self or caregiver report questionnaires instead of standardized diagnostic tools is that misdiagnosis or over/under representation of pica behaviours may be reported.

Table 18

Limitation of Studies Reported by Authors

Authors	Limitations
Ashworth et al	• The cross-sectional nature of the data makes it difficult to determine whether any of the identified factors are causes or consequences of pica. • The interRAI ID provides minimal comprehensive assessing, meaning that some factors such as substances ingested could not be interpreted. • The study is limited to individuals with ID living in institutionalized settings, with severe cognitive impairment and are between 40-50 years old.
Baheretibeb et al	• The case cannot be generalizable because it is a phenomenological discussion of a single case.
Beck & Frohberg	• None reported.
Beecroft et al	• None reported.
Bhatia & Gupta	• None reported.
Dumaguing et al	• Findings may not generalize to patients in other settings besides state facilities.
Fields et al	• Data obtained from SEED was cross-sectional, limiting causal inference. • A standardized developmental questionnaire was used to define pica, however only a single behavioural item was found to be related to pica. Therefore, the study lacked data on the clinical diagnosis and sequelae of pica. • Due to the used of caregiver questionnaires to ascertain pica behaviour, some caregivers may have over or under disclose whether their child presented with pica behaviour at home.
Funayama et al	• Small sample size, however, symptoms rarely found in patients with brain injury therefore a larger sample could not be obtained. • Due to the severe cognitive impairments within the sample, usual tools to ascertain semantic memory deficits (i.e., Pyramid and Palm Test), could not be used. • Manual techniques were used for neuroanatomical analysis.
Gundogar et al	• None reported.
Josephs et al	• None reported.
Kanamori et al	• Due to single case reporting, the difference between various treatments (i.e., trazodone, fluvoxamine, and combination of drugs) for pica in a patient with AD is not clear.
Kinnel	• None reported.
Matson & Bamburg	• None reported.
Osuji & Onu	• Including participants from institutions, rather than a community sample so that the findings could be more generalizable. • Using semi-structured instead of structured questionnaires to assess for feeding behaviours.
Stein et al	• None reported
Matson et al	• None reported

Limitations of the Systematic Review, Overall

Within the SR process conducted, there were a few limitations. First, the database search boolean phrases could have been more specific, which would have provided a more tailored search to include specific types of pica (words ending with the suffix 'phagia'). However, broad terms were used due to the limited research within the field of neurological and psychopathological correlates and pica, therefore specifying the search phrases more narrowly could have excluded some relevant studies. Second, inclusion criteria could have solely included studies in which pica was diagnosed by use of professional clinician or the DSM criteria. This would have ensured that a standardised tool, which included one set of criteria, was used for the diagnosis of pica, therefore ensuing that all studies included presented individuals with pica. Third, the two articles included in the SR, which were high risk in terms of poor methodological quality, could have been excluded during the methodological evaluation. However, these were retained due to the limited number of articles for inclusion overall, many of which were case report/series. Therefore, the findings of these journals will be interpreted with caution. Lastly, the SR only included articles written in English and did not include grey literature, which therefore excluded research from non-westernized contexts in which the predominant language is not English.

Conclusion

To conclude, the aim of this SR was to establish the neurological and psychopathological correlates of pica to better understand the possible mechanisms involved in the feeding disorder. Even though limitations were identified within the included studies as well as within the systematic review overall, the current study still contributes to understanding the possible correlates of pica. The most prevalent neurological correlates of pica in the SR included neurodegenerative diseases (FTD; AD and Multi-infarct Dementia) and ABI and stroke. The neuroanatomical region most associated with pica included the frontal and temporal cortices as well as structures involved within the limbic system (hypothalamus). Neuropsychological correlates of pica included semantic memory deficits as well as cognitive difficulties following left temporal (verbal learning, memory, and reasoning) and right frontal (cognitive switching) damage. Neurodevelopmental disorders commonly associated with pica were ID and ASD. In addition, the most prevalent psychopathological correlates of pica in the current study included OCD, schizophrenia, and depression, with the relief of anxiety being the most prominent core reasoning for engaging in pica behaviour. In the studies included, pica was treated predominantly with serotonin inhibitors or antagonists, indicating a possible correlation between the dysregulation of serotonin neurotransmitters and pica.

Even though these findings prove to be promising in identifying neurological and psychopathological correlates of pica, the studies included were predominantly case reports or case series, therefore a recommendation for larger scaled studies is warranted. In addition, within practice and future research, standardised tools and/or formal diagnostic criteria, such as those put forward in the DSM-5 TR, should be used to obtain a diagnosis of pica. Lastly, future research should aim to recruit participants from the general population, so that the findings are not only applicable to individuals who are hospitalized/institutionalised.

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Appendix A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases; registers; websites; organisations; reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases; registers and websites; including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review; including how many reviewers screened each record and each report retrieved; whether they worked independently; and if applicable; details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports; including how many reviewers collected data from each report; whether they worked independently; any processes for obtaining or confirming data from study investigators; and if applicable; details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures; time points; analyses); and if not; the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics; funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies; including details of the tool(s) used; how many reviewers assessed each study and whether they worked independently; and if applicable; details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio; mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis; such as handling of missing summary statistics; or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed; describe the model(s); method(s) to identify the presence and extent of statistical heterogeneity; and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis; meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
RESULTS			
Study selection	16a	Describe the results of the search and selection process; from the number of records identified in the search to the number of studies included in the review; ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria; but which were excluded; and explain	

Section and Topic	Item #	Checklist item	Location where item is reported
		why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes; present; for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval); ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis; briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done; present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups; describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice; policy; and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review; including register name and registration number; or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed; or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review; and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data; code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

Appendix B

Psychology Department (UCT) Ethics Committee Ethical Approval

UNIVERSITY OF CAPE TOWN

Department of Psychology

University of Cape Town Rondebosch 7701 South Africa
Telephone (021) 650 3417
Fax No. (021) 650 4104

13 May 2020

Lauren Fourie
Department of Psychology
University of Cape Town
Rondebosch 7701

Dear Lauren

I am pleased to inform you that ethical clearance has been given by an Ethics Review Committee of the Faculty of Humanities for your study, *Exploring Pica: A systematic review, a neuropsychological profile of a sample of individuals with intellectual disability.* The reference number is PSY2020-010.

I wish you all the best for your study.

Yours sincerely

Catherine Ward
Professor
Chair: Ethics Review Committee

Appendix C

JBI Critical Appraisal Tool Checklists for Study Designs

JBI Critical Appraisal Checklist fo1r Case Repo1rts

Reviewer ..... Date .....

Author ---------- Year _____ Record Number -------,

		Yes	No	Ut1cllear	Not applkalble
:t	Were patient'sdemographic characteristicsclearly described?	☐	☐	☐	
2..	Was thepatient's history clearily descrilbed and presented asa timeline?	☐	☐	☐	
3,,	Was the curirent clinical condition ofthe patient on presentation clearly described?	☐	☐	☐	
4,,	Were diagnostictestsor assessment methods at1d the results clearly described?	☐	☐	☐	
5,,	Was theinterventionjs) or treatment procedure(sl clearly described?	☐	☐	☐	
6,,	Was the post-it1tervention clit1irnl condition clearly described?	☐	☐	☐	
7,,	Were adverse events(harms) or unanticipated events identified and described?	☐	☐	☐	
8,,	Does the case report provide takeaway lessons?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

TI-IE JOANNA BRI :CS I STITUTE

JBI Critical Appraisal Checklist for Case Series

RevieiNer _____ Date _____

AI.Itihor ---------- Yea _____ Rernrd Niu lle;r _____,

	Yes	'o	Undear	ap,plicable
l_ Were there clear criteria for inclusion in the case :series?	☐	☐	☐	
2_ WaiS he rnmlition meaiSt1red in a :sta cla d, rel'iabl'e wa,; for all particij}ants indlllded in he case series?	☐	☐	☐	
3_ Were varclmB ol:ls,used for id'.enti ica1ticm of 1ille condili:ionfor an JNH1kii:@msinduc:!&I in the case :sefe.s?	☐	☐	☐	
[licl the case seriesh:ave mim erutive inclusion o1r particij}ants?	☐	☐	☐	
5_ [licl the case seriesh:ave complete i cl'.usion o particij}ants?	☐	☐	☐	
6_ WaiS. here dear reporting of tfle demo ra hicsoli 1i:hleiticiJNtlmts in tile s1i:mfy?	☐	☐	☐	
7_ WaiS. here deiar reporting o di iralliinforma1:ion of 11he participams?	☐	☐	☐	
8. Were the ol!Jtcomes or follov1up resulits of caiSes clearly reported]_	☐	☐	☐	
9_ WaiS. ere deiar reporting o tfle presei-mng site[sl/cliimicl:s],demographic infmm 1i:im?	☐	☐	☐	
10_ WaiSis. teal analvsisapprop iaie?	☐	☐	☐	☐

Overall!appraisaJ: Indude ☐ Excluo'.e Seek un:her inllfo ☐

Commeim:s,jlndud ng reason for exdusronJ

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JBIICrritiica1I Apprais,a1I Checklist for Cas,e,Contro,IStudies

Re1fe: v.e,r _____ Date _____

A1.1th.or _____ Year _____ !RecordN1.1mb e:r _____

	No	Ull'ldlear	Not applicable
1. Were the groups comparable other th,an Irie presenoe of d1sease in cases or the absence of disease il'lcontrols'? D	☐	☐	☐
2. Were cases and controls matdhed appropriatel\r? D	☐	☐	☐
3. Were the s:ame criteria1.1.sed for id;el'ltiftca1tim1o1f casesa111'1dloontrolls? D	☐	☐	☐
4. Was rexpmureme.a.sured ill'aal 111'1d!ard, vall"dand **reliable way?** D	☐	☐	☐
5. Was exposI!Ire meia.sured in the same wav for casesa111'1dloontrolls? D	☐	☐	☐
6. Were conooundingfactors id'e:l'lti ied? ☐	☐	☐	☐
J. Wer,ema eg"ec.stod'eialwithconooundi g actors stated?' D	☐	☐	☐
&. Were ou comesass:,ec.ssedlin a1mll'ld!ard, validand rel'iab'le way for casesand controliS? D	☐	☐	☐
9'. Was the**exposI!Ireperiod**of interes. **lo g** ell'lougIll to **be meani111gful?** D	☐	☐	☐
10. Was appropriate statistical **all'laly.sis** used'? ☐	☐	☐	☐

0 rerall **appraisal:** Incl'ude D Exclud'e Se;elcfurther info D

Comment:s(ll'ldlu:di111greason for excllusionl

JBII·0nitiica1I Apprais,al Checklist for Analyt: cal CrocSs Sectio,nal Studi,e,s

Reviewer Date

Alilihmr ---------- Year _____RecordNu beir_____,

	Yes	N'o	Undea	Not applicable
1. Were tlhe arn:er" fo:rinclusionin tlhe sample clearly defined?				
2. Were tlhe studysubJectsand thesetlti'ngdescribed in detail?	☐		☐	
3. Wastlhe expo,sure easuredin a vaUdandr,eliable way?	☐		☐	
4. Wer,e objective, stairndard criteria u9edfor easuremen of trne rnndition?	☐		☐	
5. Were confoundingfacbor:s,identified?	☐	☐	☐	☐
6. Were strategJies to deal withconfoundingfaoto:rs stated?	☐		☐	
7. Were tlhe outrnmes,measured in a validand reliable way?	☐		☐	
8. Was appmp:riates . tisticalanalysis used?				

Overalllappraisal: IndI!Jde ☐ Exclu:dE:☐ Seel(UlllilerilllfO

Gommeints,llndu:dllllgreasonfor exdusionl