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# Understanding urbanicity: how interdisciplinary methods help to unravel the effects of the city on mental health

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## Invited Review

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## Abstract

Twenty-first century urbanization poses increasing challenges for mental health. Epidemiological studies have shown that mental health problems often accumulate in urban areas, compared to rural areas, and suggested possible underlying causes associated with the social and physical urban environments. Emerging work indicates complex urban effects that depend on many individual and contextual factors at the neighbourhood and country level and novel experimental work is starting to dissect potential underlying mechanisms. This review summarizes findings from epidemiology and population-based studies, neuroscience, experimental and experience-based research and illustrates how a combined approach can move the field towards an increased understanding of the urbanicity-mental health nexus.

## Introduction

Urbanization is a relatively recent cultural phenomenon, starting about 10 000 years ago with the change from a human hunter-gatherer existence to intense agriculture. Cities have been on the rise and today 55% of the world's population lives in urban areas. Further urbanization is expected (UN, 2018). Living in a city may offer benefits, such as access to cultural offers and healthcare, but epidemiological studies have frequently shown that mental health problems accumulate in urban areas [e.g. Vassos, Agerbo, Mors, & Pedersen (2016); Vassos, Pedersen, Murray, Collier, & Lewis (2012)]. This suggests adverse influences of urban environments, to which humans may not be equipped given their short exposure in the evolutionary history [*Evolutionary Mismatch Hypothesis*, see Li, van Vugt, & Colarelli (2017) for an overview]. According to the biophilia hypothesis, human beings have an innate love for the natural world and a universal tendency to seek connections with other forms of life, which results at least in part from our genetic makeup and evolutionary history (Kellert & Wilson, 1993). Based on the evolutionary perspective, two theoretical frameworks have been proposed to explain the effects of natural *v.* urban encounters on the human psyche. According to Attention Restoration Theory [ART; (Kaplan & Kaplan, 1989)], urban life taxes cognitive resources, particularly directed attention, to a much greater extent than the environment our ancestors were used to in our past. Being present in nature helps to replenish this voluntary cognitive resource, because the sensory qualities of natural environments trigger non-effortful processes, particularly involuntary attention. The other framework, which may be complementary rather than exclusive, is Stress Reduction Theory [SRT, (Ulrich et al., 1991)], which emphasizes unconscious effects on the autonomic nervous system to explain how nature may reduce stress, especially the natural landscapes which were in our collective past beneficial for survival.

Investigating how the environment is associated with mental health and wellbeing requires a definition of the different components that constitute a natural or an urban environment and that may impact the human psyche. A plausible set of urban influences may lie in social characteristics, such as high population density, low social cohesion, repeated transgressions of



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personal space and high socioeconomic deprivation [for reviews see Galea & Vlahov (2005); Heinz, Deserno, & Reininghaus (2013)]. Further risk may be conveyed by the physical characteristics of cities, such as lack of green-space or environmental pollution (Attademo & Bernardini, 2017; Rautio, Filatova, Lehtiniemi, & Miettunen, 2018) and elements globally referred to as 'urban stress'. Understanding these influences requires studies that document spatial variation and investigate to what extent social and material situations are aetiologically relevant (March et al., 2008); to enable urban designs that mitigate the risk and enhance protections (Adli et al., 2017). This selective review aims to illustrate how interdisciplinary research from epidemiology, experimental psychology, neuroscience and social sciences is instrumental in achieving this goal and to suggest directions for future research.

## The urban environment and mental health

Living in or growing up in an urban environment has been associated with the elevated prevalence of mental disorders (Peen, Schoevers, Beekman, & Dekker, 2010). Most research in this realm has focussed on disorders in the schizophrenia spectrum. However, particularly in the last decade, investigations of other mental health conditions have emerged. Compelling evidence supports the urbanicity and non-affective psychosis link [OR 1.72 (Krabbendam & Van Os, 2005); meta-analytic IRRs of 1.68 (Vassos et al., 2016) and 2.25 (Castillejos, Martín-Pérez, & Moreno-Küstner, 2018)]. Findings are most robust for urban residence at birth and during childhood, suggesting an important impact of urban factors on the developing organism (March et al., 2008; Paksarian et al., 2018; Toulopoulou, Picchioni, Mortensen, & Petersen, 2017). Urban birth and provincial city upbringing have also been associated with bipolar disorder [IRR 1.18 (Marcelis, Navarro-Mateu, Murray, Selten, & Van Os, 1998), 1.21 and 1.23 (Pedersen & Mortensen, 2006)]; and urban birth and current urbanicity have been associated with the prevalence and incidence of unipolar mood disorders [e.g. IRR 1.16 (Vassos et al., 2016); pooled OR of 21 studies 1.39 (Peen et al., 2010), for a review with mixed results see Rautio et al. (2018)]. Associations with current urbanicity have also been found for anxiety disorders [pooled OR of 12 studies 1.13 (Peen et al., 2010)]. Urban residence at birth and during childhood has been associated with autism spectrum disorders [IRRs birth: 2.28; childhood: 2.85 (Lauritsen et al., 2014), birth: 1.41 (Vassos et al., 2016)]. The evidence for substance use is mixed, depending on geographic region and substance [IRRs 1.76–2.47 (Peen et al., 2010; Vassos et al., 2016), pooled OR of 13 studies 1.31 (Peen et al., 2010)]. Links between urbanicity and eating disorders were mostly, but not always inconclusive [e.g. (Mitchison & Hay, 2014), Mulders-Jones, Mitchison, Girosi, and Hay (2017), Penkalla and Kohler (2014), Vassos et al. (2016)].

Some epidemiological studies suggest that the risk of urbanicity is increased in those with a genetic liability for mental health conditions, as in the case of psychosis (Krabbendam & Van Os, 2005; van Os, Kenis, & Rutten, 2010).

At the same time, those at higher risk might be drawn towards living in urban or deprived areas [i.e. selective migration (Colodro-Conde et al., 2018; Sariaslan et al., 2016)], but such mechanisms can only explain a small part of the urbanicity effect (Paksarian et al., 2018). Given that hereditary risk for mental health disorders involves multiple common genetic variants of small effects, future studies could investigate how urbanicity interacts with polygenic risk scores. Using this approach for other environmental exposures, recent results from the EU-GEI study suggested that both early-life adversity and cannabis use interacted with molecular genetic risk state in the development of psychosis (Guloksuz et al., 2019).

Importantly, emerging evidence shows the geographic variation in the relation between urbanicity and psychosis. For instance, EU-GEI showed no significant overall association between current urbanicity and psychosis, with opposite effects in the UK and the Netherlands (IRRs = 1.17 and 1.89) and France, Spain and Italy (1.01, 1.01, 0.72) (Jongsma et al., 2018). A study of low- and middle-income countries showed higher psychosis rates with urbanicity in Estonia, but opposite patterns in Mali, Senegal and the Philippines (DeVylder et al., 2018). For affective psychosis, some reported a lower incidence with urbanicity (Kelly et al., 2010; Kirkbride et al., 2017) and living in urban environments or higher unit density neighbourhoods has been associated with a lower incidence of depression and anxiety in Peru and the USA (Loret de Mola et al., 2012; Miles, Coutts, & Mohamadi, 2012). This variation in risk for different disorders, time of exposure (e.g. developmental *v.* current) and geographic region stresses the need for systematic research that assesses periods of risk in conjunction with multiple individual (e.g. polygenic risk) and contextual factors (e.g. specific risk attributes of urban environments). The key epidemiological findings are summarized in Box 1.

**Box 1.** Epidemiological findings

- Urbanicity has frequently been associated with an increased risk for mental health disorders, with most compelling evidence for non-affective psychosis, followed by affective-, autism spectrum- and anxiety disorders. Less and more equivocal evidence exists for substance use-, eating- and other disorders
- Negative effects appear most pronounced for childhood urbanicity
- New evidence shows that urbanicity effects are context specific (e.g. as indicated by absent or reversed effects for psychosis in southern European countries)

## Risk attributes of the urban environment

Urban risk does not only lie in population density, but arises from an accumulation of social and environmental stressors (Galea, 2011; Rapp et al., 2015; see Box 2).

*Social and economic factors*, such as deprivation/poverty and social fragmentation, lack of social capital, cohesion and trust may explain urban risk [(Castillejos et al., 2018; Drukker, Krabbendam, Driessen, & van Os, 2006; Galea et al., 2007; O'donoghue et al., 2016; Zammit et al., 2010), for reviews see De Silva, McKenzie, Harpham, & Huttly (2005); Ehsan & De Silva (2015); McKenzie (2008)]. Yet, some contradictory evidence shows higher social cohesion and incidence of distress and common mental health disorders in rural areas (Loret de Mola et al., 2012). Overall, similar rates of poverty and social exclusion have been reported in urban and rural European areas, yet there were regional variations with higher social exclusion and inequality particularly in western European cities (Eurostat, 2016). This is interesting, as perceived social inequality has been suggested to increase the risk for

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**Box 2.** Hypotheses on urban risk attributes

- *Environmental pollution*: proposes that pollutants, such as heavy metals impact negatively on (mental) health (e.g. through their effects on the nervous system)
  - ✓ Supporting correlational evidence on the link between pollution and risk for mental health conditions exists; however, effects are small at least in the case of psychosis
  - ✓ Traffic pollution has been associated with altered neural connectivity in humans
  - ✓ Animal studies support toxic effects of pollution and link it to depressive-like behaviours
- *Lack of nature space:* proposes that being in nature (e.g. green space) has salutogenic effects, for instance through cognitive restoration or stress reduction, which re-calibrate psychological and physiological systems
  - ✓ Urban upbringing has been associated with less efficient neural processing on a cognitive task for working memory
  - ✓ Proximity to green space has been linked to grey and white matter volume changes in young and old individuals
  - ✓ Visiting green spaces or nature experiences in cities positively affect mental health-related factors, such as mood and cognition
  - ✓ Brief nature experiences change physiological health markers and rumination-related brain activation
- *Selective migration:* posits that the increased rates of mental health problems observed in cities are due to selective influx of people who are predisposed to develop a disorder
  - ✓ Research in psychosis shows some effects of polygenic risk on city living and neighbourhood poverty; however, the genetic associations may only account for a small part (~2%) in schizophrenia risk
- *Social stress*: proposes that urban environments are defined by a high occurrence of social stressors (e.g. transgression of personal space, low SES and inequality, social exclusion, instability and defeat) that render vulnerable individuals at risk
  - ✓ *In situ* studies show that threat perception is associated with neighbourhood affluence, the mental health status of the perceiver and that individuals with psychosis experience unchosen social interactions in cities as stressful
  - ✓ City living has been associated with higher activation of stress-related brain areas during stress-tasks
  - ✓ Social stress (although not necessarily urbanicity related), has been linked with structural and functional brain alterations

mental distress, especially when the situation is unchangeable [*Social Defeat Hypothesis* (Selten, van der Ven, Rutten, & Cantor-Graae, 2013)]. Social defeat could explain elevated risk in low socio-economic status (SES)/higher inequality neighbourhoods, which might be more typical, yet not specific to cities (Blumenthal & Kagen, 2002). Further, densely populated urban areas are characterized by a high frequency of social encounters. These may contribute to negative urban effects for individuals with a liability for mental health conditions through increased stress sensitivity (Myin-Germeys, Delespaul, & Van Os, 2005) and/or, as in case of psychosis and depression, deficits in social cognition (Green, Horan, & Lee, 2015; Weightman, Air, & Baune, 2014).

A factor that has frequently been investigated in the context of urban risk is migration, which is thought to increase the risk through social instability (Bhugra, 2004; Cantor-Graae & Pedersen, 2013; McKenzie, 2008; Price, Dalman, Zammit, & Kirkbride, 2018). However, migrant status is not a risk *per se* and its effects vary between countries and ethnic groups (Jongsma et al., 2018; Kirkbride et al., 2017; Schofield et al., 2017). Social support structures, shared social history, positive identification with one's own ethnic group (Anglin, Lui, Espinosa, Tikhonov, & Ellman, 2018; Veling, Hoek, Wiersma, & Mackenbach, 2010) and low discrimination appear to render individuals more resilient (Schofield et al., 2017; Veling et al., 2008) showing that effects of individual characteristics (e.g. migrant status) depend on context. Finally, it is important to consider that the perception of the social stress associated with the urban environment is also influenced by the mental health and wellbeing of the individual (Corcoran et al., 2017). For example, a large population study in adolescents showed that those who perceived higher levels of threat in their neighbourhood were more likely to have psychotic experiences (Newbury et al., 2018). This effect remained after accounting for levels of crime, individual disorder, neighbourhood- and family-level SES, suggesting that the subjective perception of the urban environment is an important target for research and possibly intervention.

An important *physical factor* through which cities could impact mental health may be lack of green space (Bratman, Hamilton, & Daily, 2012; Fong, Hart, & James, 2018; Gascon et al., 2015; Lee & Maheswaran, 2010; van den Berg et al., 2015). Low compared to high green space presence was associated with a 1.52-fold increased schizophrenia risk in a Danish case registry study (Engemann et al., 2018), with most profound effects for low green space presence during early childhood. Moreover, individuals with psychosis have been found to reside in less green areas than the general population (Boers, Hagoort, Scheepers, & Helbich, 2018). Lack of green space has also been associated with the prevalence of anxiety and autism spectrum disorders (de Vries et al., 2016; Wu & Jackson, 2017), but findings are mixed for mood and substance use disorders (Banay Rachel et al., 2019; de Vries et al., 2016).

As a flipside to reduced green space, the features of urban environments (e.g. noise, light, social encounters) may lead to cognitive overload for attention, memory or cognitive control (Bratman et al., 2012) and salience processing in general (Winton-Brown, Fusar-Poli, Ungless, & Howes, 2014). Some evidence linked urbanicity to reduced cognitive development in children (Gouin et al., 2015). Schizophrenia risk has been associated with lower cognitive functioning and urbanicity, possibly indicating reduced coping ability with the eventfulness of cities (Weiser et al., 2007). Noise pollution or noise-induced stress has also been associated with measures of annoyance, displaced aggression, reduced wellbeing and cognitive functioning (Dzhambov & Dimitrova, 2014; Goines & Hagler, 2007; Ohrstrom, 2004; Wright, Peters, Ettinger, Kuipers, & Kumari, 2014). In line with the biophilia hypothesis (Kellert & Wilson, 1993), these findings may pinpoint impaired relaxation (e.g. SRT) or cognitive restoration (e.g. ART), which are associated with nature sights and sounds or reduced cognitive load (Berto, 2014; Bratman et al., 2012). Often exposure to noise occurs simultaneous to exposure pollutants from road or air traffic, which might be an independent mechanism that transduces urban risk [e.g. exposure to ultrafine particles, heavy metals as lead and cadmium, or nitrogen oxide (Buoli et al., 2018; Newbury et al., 2019), which affect particularly individuals with lower SES in urban areas (Cesaroni et al., 2010; Laurent, Bard, Filleul, & Segala, 2007)]. Though, a recent review suggested that pollution only accounts for a small part of the risk for mental health problems, at least in psychosis (Attademo, Bernardini, Garinella, & Compton, 2017).

Other, possibly related, salutogenic effects of natural environments could include better immune function, lower blood pressure and/or health behaviours, such as physical and social activity, which directly affect the individuals and unborn offspring (Ebisu, Holford, & Bell, 2016; Fong et al., 2018; James, Banay, Hart, & Laden, 2015; Kuo, 2015; Maas, van Dillen, Verheij, & Groenewegen, 2009; Rook, 2013; Rook, Lowry, & Raison, 2013; Twohig-Bennett & Jones, 2018). Interestingly, visiting green spaces appears to affect the mental health of city dwellers positively (Alcock, White, Wheeler, Fleming, & Depledge, 2014; Bratman, Hamilton, Hahn, Daily, & Gross, 2015). Lack of green space during upbringing and adult life could be due to various SES-related factors, but low use of green space could lie in reduced motivation and withdrawal from activity that accompanies mental health conditions (Van den Berg et al., 2016), highlighting the potential importance of activating interventions.

In sum, studies on urban upbringing and current urban living show that a variety of individual and context-related factors of the urban environment increase the risk for mental ill-health. A common denominator of urbanicity risk appears to lie in the presence of stressors and the lack of opportunity for stress relief associated with specific social and physical characteristics of the urban environment (Gong, Palmer, Gallacher, Marsden, & Fone, 2016). Importantly, the urban environmental risk factors may cluster and have additive, if not synergistic effects (Kuepper, van Os, Lieb, Wittchen, & Henquet, 2011; Morgan et al., 2014), which require further systematic investigation of the interplay of social, environmental and person characteristics.

## The urban environment and the brain

Neuroscientific studies may contribute to our understanding of the neurobiological processes mediating the effect of urban living on mental health (Meyer-Lindenberg & Tost, 2012). For instance, neuroimaging can investigate hypothesized emotional and cognitive brain mechanisms or brain areas and connections that are susceptible to urban effects. The social stress hypothesis is supported by an initial functional neuroimaging (fMRI) study that probed the blood-oxygen-level-dependent (BOLD) brain to stress as a function of urban upbringing and current city living. In healthy individuals, current city living was associated with higher activation of the amygdala during social stress. Urban upbringing moreover was associated with an increased activity of the perigenual anterior cingulate cortex (pACC), which connects to frontal and limbic brain areas and has been implicated in emotional processing, contingency learning and cognitive control (Stevens, Hurley, & Taber, 2011; Palomero-Gallagher et al., 2018). In another study, current city living was associated with higher activation of the amygdala, medial orbital cortex and pACC during a task measuring reward activation and modulation (Krämer, Diekhof, & Gruber, 2017). The results indicate a fronto-limbic hypersensitivity during stress and reward processing. The finding is in line with the hypotheses derived from experimental and epidemiological studies, which suggest that exposure to urban (social) stress leads to neural sensitization and sensitization of physiological stress systems as the hypothalamus–pituitary–adrenal axis (Selten & Cantor-Graae, 2005; Selten et al., 2013; Steinheuser, Ackermann, Schonfeld, & Schwabe, 2014). In addition, urban upbringing has been associated with less efficient prefrontal processing during a working memory task, suggesting the involvement of cognitive control processes (Reed et al., 2018). Although the evidence is still limited, structural neuroimaging associated urban upbringing with reduced dorso-lateral prefrontal cortex (dlPFC) and (in men only) pACC volumes (Akdeniz et al., 2017; Haddad et al., 2014), reduced cortical thickness in frontal and temporal–parietal cortices and increased volume of the precuneus (Besteher, Gaser, Spalthoff, & Nenadić, 2017; Lammeyer, Dietsche, Dannlowski, Kircher, & Krug, 2019), as well as white matter changes in the left superior longitudinal fasciculus (Lammeyer et al., 2019). Few studies have linked urban living to brain phenotypes in disorder. In males with a psychotic disorder, urban upbringing was associated with reduced grey matter volume (Frissen, van Os, Peeters, Gronenschild, & Marcelis, 2018), but not with cortical thickness (Frissen et al., 2017), or functional connectivity (Peeters et al., 2015). Importantly, it is largely unclear what accounts for these neural alterations. Initial studies, which are discussed in the following paragraph, have focussed on social stressors and green/blue space as potential explanatory factors of structural and functional brain changes.

An important new direction is the study of gene–urbanicity interactions for brain phenotypes. In a subgroup of the sample studied in Lederbogen et al. (2011), a functional variant of the neuropeptide S receptor 1 interacted with urban upbringing on the amygdala stress response during the social stress task (Streit et al., 2014). Urban upbringing also interacted with dopamine genes in altering prefrontal function during a working memory task, a finding that was replicated in two independent samples (Reed et al., 2018). Future studies of gene–urbanicity interaction could capitalize on the identification of polygenic risk scores for the disorder as an index of molecular genetic risk, rather than focusing on single nucleotide polymorphisms.

In sum, initial evidence links urbanicity to changes in neural activation and structure. While tentatively supporting existing theories, the findings need to be interpreted with great caution given their correlational nature. It will be important for future research to draw upon insights from the animal literature and to directly investigate the impact of different urban attributes on the brain in experimental and experience-based studies. Initial studies that attempted to directly unravel the effects of the city will be discussed in the following paragraph.

## Risk attributes of the urban environment and the brain

Many studies have investigated neural correlates of social phenomena that are relevant to the hypothesized mechanisms of urbanicity, although not explicitly framed in this context. For example, low childhood SES has been associated with a range of brain structural and functional changes (Farah, 2017; McDermott et al., 2019), with the strongest effects in the most disadvantaged children (Noble et al., 2015). A quantitative meta-analysis of social environmental stressors based on 54 studies and 3044 participants concluded that the experience of social environmental stress was associated with an altered BOLD response across several brain regions. Increased BOLD of the right amygdala was a robust finding across multiple studies (Mothersill & Donohoe, 2016). This effect was similar for the ($n = 34$) studies including adults and those including children/adolescents ($n = 21$). The meta-analysis included different types of social stressors, some of which are not relevant to urban social risk (e.g. childhood trauma), but are nevertheless informative on

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the key role for the amygdala in the neural effects of the social environment. Finally, recent evidence linked psychosocial stressors (childhood adversity, migration and urban living) in healthy volunteers to reduced volume of the amygdala (Weissman et al., 2019) and increased connectivity between striatal and cortical regions, involved in salience and reward processing (McCutcheon, Bloomfield, Dahoun, Mehta, & Howes, 2019). In addition, evidence from the animal literature shows that repeated social defeat is associated with sensitized neurons and microglia over several weeks (Weber et al., 2019). Such changes at cell level might drive higher-level changes in brain structure, and could contribute to various mental health conditions that have been associated with stress sensitization and reward processing deficits (Gerin, Hanson, Viding, & McCrory, 2019; Weissman et al., 2019; Whitton, Treadway, & Pizzagalli, 2015).

Future studies could apply more detailed methods to assess the experience of social stress in urban and rural neighbourhoods, as is already done in epidemiological studies [e.g. Binbay et al. (2012)], allowing for a comparison of groups that differ on well-defined social dimensions of residential environments. Social cognitive neuroscience has developed validated paradigms that could be used in conjunction with this approach to study how individuals with different urban social experiences respond to social stressors. For example, the experience of social exclusion, social inferiority or transgression of personal space can be experimentally induced and studies using these paradigms have reliably associated negative social experiences with activation in brain areas that are involved in the processing of negative emotions and cognitive control (Kennedy, Gläscher, Tyszka, & Adolphs, 2009; Kishida, Yang, Quartz, Quartz, & Montague, 2012; Zink et al., 2008).

Recent studies have started to investigate the associations between urban physical factors and the brain. Kühn et al. (2017) used data on green and blue space from the European Urban Atlas in conjunction with structural brain imaging, and reported that older adults who lived close to forests had increased amygdala integrity, based on three different neuroimaging sequences of grey and white matter density (voxel-based morphometry, mean diffusivity from diffusion tensor imaging and magnetization-transfer ratio). The study also investigated associations with urban green, water and wasteland and additional regions of interest, the pACC and dlPFC, for which volume reductions have previously been linked to urban upbringing (Akdeniz et al., 2017; Haddad et al., 2014). However, none of the other associations was significant, suggesting that neuro-regenerative effects of nature are specific to (non-urban) green space and primarily working on brain regions that are implicated in emotional (threat) processing, rather than those related to cognitive control. It is possible that non-urban green space is a proxy for personal space (i.e. low social exposure), which is likely to act positively on the brains' threat system. Although, others showed that lifelong access to residential greenness (using satellite-based normalized difference vegetation index) was positively associated with grey and white matter volume in prefrontal and premotor areas and the cerebellum in school-aged children (Dadvand et al., 2018), possibly relating to neural plasticity and regeneration. Interestingly, the regions that were associated with greenness were also positively associated with working memory and inversely associated with inattentiveness, suggesting that impaired structural integrity could underlie the previously discussed cognitive effects of urban environments [e.g. (Reed et al., 2018)]. Others found that in children between 8 and 12 air pollution exposure was mainly associated with reduced functional connectivity in the default mode network activity and stimulus-driven mental operations (Pujol et al., 2016) rather than structure or membrane metabolites, which might point toward stress-related mechanisms. Neurotoxicity-related structural changes, as supported by animal studies (Fonken et al., 2011; Levesque, Surace, McDonald, & Block, 2011), could appear further down the line of development.

The initial neuroimaging studies suggest stress sensitization through environmental stressors, neurotoxicity and neuro re- and degeneration as possible neurobiological pathways that mediate urbanicity effects on cognitive functioning and mental health. Future studies need to systematically investigate multiple mechanisms that could underlie the urban effect on the brain (e.g. exposure to toxic or noise pollution, social stressors). Longitudinal research will be necessary to unravel developmental effects. To improve our insight into which specific urban features are involved, experimental and experience-based studies that investigate immediate responses to specific physical and social characteristics of urban environments will be indispensable.

## *Experimental and experience-based studies: testing causality of urban factors*

*Experimental studies* use randomized designs to investigate the psychological or psychophysiological effects of nature/urban-related experimental stimuli or short-term experience of nature or urban environments. Drawing on ART and SRT, these studies have included cognitive outcomes as well as outcomes related to mental health and psychophysiology. Studies differ in type (e.g. images *v.* actual presence) and duration (e.g. minutes to hours) of the nature *v.* urban experience, but overall systematic reviews confirmed the positive effects of nature on mental wellbeing and cognition, although some studies yielded inconclusive findings (Bowler, Buyung-Ali, Knight, & Pullin, 2010; Bratman et al., 2012; Ohly et al., 2016). The effects on psychophysiological indicators, such as blood pressure and heart rate variability, are less well-studied (Bowler et al., 2010). However, there are individual studies that suggest that a brief experience of nature changes physiological health markers (Li et al., 2011; Park, Tsunetsugu, Kasetani, Kagawa, & Miyazaki, 2010), an effect that may extend to simulated environments (i.e. viewing nature *v.* urban scenes) (Brown, Barton, & Gladwell, 2013). Moreover, positive effects on mood and cognition of a short walk in nature *v.* urban environments have been observed in individuals with major depression (Berman et al., 2012). The experimental approach has also been applied to study the effects of specific urban environments. For example, passing through a deprived urban environment increased anxiety and reduced trust in patients with persecutory delusions (Ellett, Freeman, & Garety, 2008), as well as in healthy individuals (Nettle, Pepper, Jobling, & Schroeder, 2014). In patients with persecutory delusions, going out in a busy shopping area had similar effects (Freeman et al., 2014).

Recently, studies also started to investigate the direct neural effects of short-term urban *v.* nature experience. Healthy participants underwent resting-state fMRI before and after a 90 min walk in a nature as opposed to an urban environment (Bratman et al., 2015). The walk in nature reduced self-reported rumination and activation in the sub-genual prefrontal cortex (sgPFC), whereas the urban walk did not. The sgPFC is linked to self-focused behavioural withdrawal and rumination, supporting a

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restorative effect of nature, possibly by distracting participants from negative feelings. It is important to note that the exposure conditions should be carefully matched for characteristics that are not directly related to nature or urban environments, such as pleasantness or level of threat. That is, unpleasant nature scenes may well have marked negative effects (Pretty, Peacock, Sellens, & Griffin, 2005), just as beautiful urban scenes may have positive effects (Seresinhe, Preis, MacKerron, & Moat, 2019). A solution to this problem would be simulated exposures that are matched for such characteristics. Virtual reality has successfully been applied to study the effect of social environmental stress in psychosis, and may combine experimental control with good ecological validity (Veling et al., 2008), for a systematic review see Valmaggia, Day, and Rus-Calafell (2016).

In sum, there is convincing evidence for positive effects of the short-term experience of nature on wellbeing and cognition, which may occur through largely unconscious processes affecting attention and autonomous nervous system activity. The experimental approach may be instrumental in identifying specific associations between elements of natural or urban environments and outcomes that are relevant to mental health. At the same time, not all relevant elements of natural or urban environments lend itself to experimental designs with human participants (e.g. pollution) and it is unclear how short-term effects relate to the effects of years of exposure. Within these constraints, future research could set out to systematically delineate the optimal duration and type of the nature experience (e.g. Barton & Pretty, 2010; Bratman et al., 2012). Furthermore, it would be relevant for experimental studies to systematically incorporate individual differences in sensitivity to the natural or urban environment, for example, related to baseline mental health, as epidemiological research points to person–environment interactions. It has also been postulated that explicit cognitions (e.g. connectedness to nature) may mediate the beneficial effects of nature experiences on attention and mental health (Mayer, Frantz, Bruehlman-Senecal, & Dolliver, 2008). Zooming in on the conscious experience of the natural or urban environment to understand the impact of the environment on the psyche is at the focus of the experience-based approach that is discussed next.

*Experience-based studies* start from the notion that the lived experience and sense-making of subjects are crucial for analysing the effects of urban or natural milieus on mental health. Therefore, the role of natural and urban environments in mental health needs to be understood as the result of people's actions and experience in context (Cresswell, 2014). Such *in situ* experiences can be captured by studies in which individuals provide quantitative and/or qualitative information, while they walk through specific neighbourhoods or natural landscapes. This may provide a much more fine-grained insight into how the effects of urban stressors identified in epidemiological studies depend on specific contexts (Söderström et al., 2016).

Corcoran et al. (2018) collected data on walkers' *in situ* judgements of threat and trust in two urban neighbourhoods, which differed in terms of deprivation. Perceptions of trust and threat were influenced by the perception of neighbourhood affluence, but also by the mental health and wellbeing of the walkers. Experience-based studies may further elucidate specific features of the urban environment that elicit stress in individuals with psychopathology. For example, a recent study used video recordings of patients' urban walks in conjunction with video-elicitation in patients with first-episode psychosis and showed that situations of stress are related to demographic density, sensory environments (in places like shopping malls), obstacles to fluid pedestrian mobility and unchosen social interactions, whereas creating sensory 'bubbles', programming mobility and creating places of comfort were tactics used to handle urban stress (Söderström et al., 2016; Söderström, Söderström, Codeluppi, Empson, & Conus, 2017). Interestingly, density, a known stressor, served as a protective context for one individual with psychosis, because being in an anonymous crowd (in contrast to being with close friends and relatives) triggered feelings of belonging without being too exposed. Other studies based on ethnographic data have shown that 'niches' (Bister, Klausner, & Niewöhner, 2016) or 'atmospheres' (Duff, 2016; Söderström et al., 2016; Söderström et al., 2017) of recovery are important for urban mental health, despite urban changes which very often reduce such possibilities for economically precarious people. These findings converge with those of recent studies in psychology on the role of space in mental health (McGrath & Reavey, 2018).

Recently, the study of the experience of the city has been complemented by the use of Ecological Momentary Assessment (EMA; Shiffman, Stone, & Hufford, 2008), which involves the repeated sampling of current experiences in real-time and real-world contexts. EMA has high ecological validity because assessments are made in the natural flow of real life and in different situations, which makes it possible to understand the variability in mental states in relation to the environment, without explicit reflection on these relationships from the side of the individual. Applying EMA, Bakolis et al. (2018) observed that specific natural features of the built environment (i.e. seeing trees, hearing birds sing) were associated with higher levels of mental wellbeing, which lasted for several hours and which was more prominent in individuals with higher trait impulsivity (Bakolis et al., 2018). EMA can be enriched with geographically explicit information (i.e. GEMA; Kirchner & Shiffman, 2016) through combination with global positioning systems and geographic information systems. By linking subjective experiences with objective measures of mobility and place, GEMA can reveal continuous and dynamic interactions between people and place. For example, focusing on the relation between location and stress in adolescents, a recent GEMA study suggested that being around urban green space was associated with lower stress (Mennis, Mason, & Ambrus, 2018). This may point to the restorative effects of nature experience, or to the tendency to seek out urban green spaces at times of lower stress, or explicitly for purposes of stress reduction. Recent advances in portable neuroimaging greatly enrich the possibilities to experimentally investigate the neural correlates of nature and urban encounters, e.g. with mobile EEG devices while participants walk in urban *v.* nature environments and talk about their experiences, an approach which has recently successfully been piloted in older individuals (Tilley, Neale, Patuano, & Cinderby, 2017).

In sum, experience-based studies provide a richness of quantitative and qualitative detail about the interactions between contextual characteristics and individual reflexive experiences. Combined with measures that tap autonomous nervous system activity, or even brain electrical activity, this may contribute to a much more fine-grained understanding of the relation between presence in urban or nature environments and mental health. These studies are suited to analyse how combined features of the milieu – constituting 'the urban' – affect people's experience and less suited to investigate the effects of isolated risk factors.

## Conclusions and future directions

A vast epidemiological literature has investigated associations between urbanicity and mental health, linking urban birth, upbringing and current residency to adverse mental health outcomes. The fact that urbanicity affects outcome across diagnostic boundaries suggests that research in this area could benefit from applying a dimensional rather than a categorical approach to psychopathology (Galea, Uddin, & Koenen, 2011; Johnstone et al., 2018). This echoes calls from other areas of research into the causes of psychopathology (Caspi et al., 2014), for example, psychiatric genetics (Selzam, Coleman, Caspi, Moffitt, & Plomin, 2018; State & Levitt, 2011). The epidemiological studies further indicate that urbanicity is not universally negative (DeVylder et al., 2018; Jongsma et al., 2018). Mixed findings are emerging between north and south and high- and middle/low-income countries. However, comparisons between studies remain difficult given the variable operationalization of urbanicity in terms of population density or urban/rural categories (city, town and village). Progress in this area comes from studies that characterize the urban environment in more detail, i.e. not only in terms of population density, but also in terms of physical and social dimensions of the urban that may be relevant to mental health. Interdisciplinary approaches between psychiatry and the social sciences encourage research to move beyond the limits of epidemiology and of urban living reduced to the vague and general concept of urbanicity and 'urban stress' (Söderström, 2019). These interdisciplinary endeavours do not necessarily have to erase epistemological differences between the life sciences and the social sciences. Instead, they may use these differences to co-create research designs. This may, for example, inspire human geographers to move beyond social constructivism and include biological dimensions of mental health (Winz & Söderström, 2020). It may help epidemiologists and neuroscientists to consider urban life as a series of situational phenomena that people encounter and actively construct, rather than something that can be reduced to the notion of 'exposure' to an invariable environment (Söderström, 2019).

Neuroscientific studies use these insights to elucidate the neurobiological pathways that mediate the effects associated with these specific physical and social components of urban life. Although this literature is still in its infancy, studies have identified candidate brain phenotypes that offer initial neurobiological support for associations between urban factors and structure and function of several brain areas, including networks associated with stress and emotion processing and regulation.

Experimental studies may buttress the correlational findings from epidemiological and neuroscientific approaches by enabling causal inferences through randomized controlled designs. Studies using this approach have shown beneficial effects of nature compared to the urban experience, and negative effects of deprived and busy urban environments. These studies may be further enriched by experience-based approaches that focus on *in situ* experience of the environment and capitalize on the notion that the way the city is lived is key to understanding the psychological and physiological responses it elicits. However, not all urban phenomena are suitable for experimental manipulation in humans (e.g. pollution), or open to introspective evaluation (e.g. immune function). In addition, experimental and experience-based studies are limited for the time being to outcomes that show immediate effects (i.e. changes in physiological and psychological parameters of stress, wellbeing, cognition), and whether these immediate effects translate to the effects of long-term urban living remains an open question. Environmental epigenetics suggest that urban characteristics (e.g. stress through exposure to pollution or social density) biochemically influence the phenotypical development and might help to understand delayed temporality and intergenerational urban effects in future research (Guthman & Mansfield, 2012).

**Box 3.** Directions for future research

- Variation in risk for different disorders, by time of urbanicity exposure, and geographic region warrants further research that would benefit from a trans-diagnostic approach
- Neuro-physiological effects of the immediate exposure to unpleasant and pleasant nature *v*. urban environments should be studied in experience-based or neuroscience settings, to overcome limitations of correlational evidence
- Effects of social urban stressors can be further scrutinized using; e.g. social neuroscience paradigms or portable Electroencephalography (EEG) to assess effects on the brain and physiological, as well as psychological indices of stress
- A wider and more systematic utilization of (geographically enriched) Ecological Momentary Assessment and mobile EEG will help to pinpoint immediate effects of person-by-place interactions in urban and rural environments
- Experimental studies in humans are not possible to study pollution, but more systematic investigations of health outcomes depending on the duration of exposure to toxins, as well as toxin concentration are possible and needed
- Approaches using agent-based-modelling will aid the understanding of multiple interacting urban factors on mental health

Urbanicity effects are complex and while it is clear that there is no silver bullet, together these studies highlight the need for multi-method interdisciplinary collaborations to elucidate multiple interacting pathways and reciprocal relations of the urbanicity–mental health conundrum. This review largely focused on contributions from psychiatric epidemiology, experimental studies and neuroscience to the understanding of urbanicity effects on mental health, and illustrated how other disciplines, which aim to understand urban life and its effects on humans, such as sociology, anthropology, urban planning or geography, will be important in future research collaborations and to create urban spaces that influence mental health positively (Baumann et al., 2019). Understanding urbanicity effects requires a complex system approach to model multiple interacting processes at individual and social levels (Galea, Riddle, & Kaplan, 2010). Specifically, agent-based models (ABM) are computer simulations which allow multiple interactions at the level of the individual or the agent (e.g. biological and behavioural characteristics, SES) and social factors (e.g. neighbourhood social and physical characteristics, mental health service facilities), that aggregate to create unexpected patterns of population health (Tracy, Cerdá, & Keyes, 2018). ABM allow researchers to investigate how specific interactions between individuals generate a collective pattern and may be particularly helpful to model the effect of interventions that cannot easily be investigated experimentally in the real world. For example, Yang, Diez Roux, Auchincloss, Rodriguez, and Brown (2011) used ABM to model walking behaviour in a city as a function of individual and environmental characteristics, and to investigate the effects of potential interventions at the individual and city level. ABM may also be used to model the effects of simulated scenarios (e.g. specific individual or environmental interventions) and examine outcomes of these interventions under different conditions. There is still much conceptual and methodological work to be done to successfully apply ABM to urban mental health, for example, in finding the balance between simplified and realistic models, and in estimating the model parameters using the available empirical data. However, epidemiological, neuroscientific, experimental and experience-based approaches may together with computational modelling advance our understanding of the impact of the metropolis on mental health, and ultimately develop evidence-based interventions towards a healthy environment (see Box 3).

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