

Using Ambulatory Assessment for experience sampling and the mapping of environmental risk factors in everyday life

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Keywords

Ambulatory Assessment, GPS-triggered e-diaries, geoinformatics, mental health

Summary

Background: Psychiatric research is increasingly interested in the influence of social and environmental contexts on human health. According to recent findings, specific impacts of urban upbringing relate to the heightened prevalence of mental disorders. Although this is a major societal problem, it remains unknown which environmental components (e.g., psychosocial stressors, rare nature exposure) are responsible. **Method:** We introduce Ambulatory Assessment (AA) as a methodological approach to investigate contextual influences. GPS-triggered electronic diaries are suitable to capture data in everyday life, gathering information on both context and mental states to assess dynamic processes in real-life and real-time. **Result:** A longitudinal study at the Central Institute for Mental Health in Mannheim combines AA, fMRI and epigenetic approaches to investigate environmental factors influencing mental health. The findings might be incorporated in urban planning to reduce mental disorders.

Schlüsselwörter

Ambulantes Assessment, GPS-triggered e-diaries, Geoinformatik, psychische Gesundheit

Zusammenfassung

Hintergrund: Die Untersuchung von Kontexteinflüssen auf die psychische Gesundheit gewinnt in der psychiatrischen Forschung an Bedeutung. Aktuelle Studien legen die Vermutung nahe, dass der Einfluss der Urbanität auf die neuronale Stressverarbeitung für die erhöhte Prävalenz psychischer Erkrankungen in Städten verantwortlich ist. Obwohl psychische Erkrankungen ein bedeutendes gesellschaftliches Problem darstellen, sind die kausalen Wirkmechanismen bisher weitgehend unerforscht. **Methode:** Ambulantes Assessment (AA) bezeichnet eine Methodengruppe zur Untersuchung von Patienten in Echtzeit. Spezielle elektronische Tagebücher (GPS-triggered e-diaries) ermöglichen die Aufzeichnung von Kontextparametern und der dazugehörigen subjektiven Symptomatik im Alltag. Damit können dynamische Prozesse in der Lebensrealität sowie in Echtzeit erfasst und geoinformatisch mit Risikofaktoren (bspw. Luftverschmutzung, Lärmaufkommen) kombiniert werden. **Ergebnis:** Eine Längsschnittstudie am Zentralinstitut für Seelische Gesundheit in Mannheim kombiniert AA, fMRI und epigenetische Untersuchungen, um Risikofaktoren ausfindig zu machen. Die Einbeziehung der Ergebnisse in Stadtplanungen soll dazu beitragen, die Anzahl psychischer Erkrankungen zu reduzieren.

Ambulantes Assessment – eine innovative Methodik zur Erfassung psychischer Symptome und Umweltrisiken im Alltag

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The interest in the influence of social and environmental contexts is continually increasing in psychiatric research. This is not surprising; in general, behaviour, human experience and psychopathological symptoms are heavily influenced by contextual variables, such as the time of day, social interactions, and location. In our view, however, two concepts should be distinguished, even though they might be related in the long run. On the one hand, present behavior and symptomatology is affected by the current context. For example, depressive symptoms vary systematically according to interpersonal context, current activities and the time of the day (44). Similarly, psychotic symptomatology correlates with interpersonal context and current activities (6). Studies that assess and/or manipulate context, like those on social exclusion (13), belong to this line of research. On the other hand, long-term exposure to contexts is also of interest. One of the best established examples is the heightened rate of schizophrenia for city dwellers compared with their rural counterparts; empirical evidence even suggests a dose-dependent relationship between psychosis risk and the duration and magnitude of the exposure to urban environments during development (23, 37).

The heightened schizophrenia risk in the context of urban upbringing has been demonstrated multiple times, but its underlying causal factors are poorly understood. The urban landscape is highly complex and heterogeneous, and there are a multitude of environmental influences that aggregate and interact in the city, such as psychosocial stressors, air pollutants, (lack of) nature experience, and poverty, among others. However, identifying the mechanisms of the most relevant factors might influence city planning and ultimately reduce the risk of mental disorders. The high burden and prevalence of psychiatric disorders and the growing numbers of people living in cities emphasize the importance of this societal problem.

Although scientists just started to unravel the complex interactions between psychopathological symptoms and environmental as well as social contexts, we are, fortunately, in the midst of an unparalleled technological advancement, with multi-sensor mobile wireless connected devices becoming ordinary among the general population. Devices such as smartphones enable us to gather and understand context-dependent psychopathological symptoms in real-time in everyday life. Furthermore, we can use this information to unravel the influence of long-term environmental exposures on psychiatric symptoms.

In the following, we will a) describe a methodological approach, Ambulatory Assessment, capable of assessing symptomatology and context in daily life, b) point to recent advances for gathering environmental information using geoinformatics, c) report on GPS-triggered elec-

tronic diaries to assess symptom-context relations in real-time in everyday life, and d) use an ongoing psychiatric study to illustrate the reported methodological aspects.

Ambulatory Assessment

Ambulatory Assessment (AA) is an umbrella term describing a wide range of methodological approaches used to study behavioral, biological and physiological processes in peoples' everyday life (15, 38); see also the definition of the Society for Ambulatory Assessment: <http://www.ambulatory-assessment.org>. AA comprises the Experience Sampling Method (e.g., paper-and-pencil diary), Ecological Momentary Assessment (e.g., electronic diary (35)), and monitoring of physiological function, environmental parameters, and physical behavior using different types of sensors such as accelerometers, GPS, or ECG.

AA allows for bypassing several limitations of traditional assessment approaches (e.g., questionnaires or clinical interviews), namely the dependence on retrospective self-reports and artificial laboratory settings. In detail, AA enables researchers to a) collect data in real-world settings, thereby making it possible to capture additional contextual information like environmental characteristics that may influence experience (i.e., time of day, location, social interaction), b) collect multiple assessments within a certain timeframe, which allows analyzing and modeling within-subject processes like affective instability or stress reactivity (29, 32), c) gather data in real-time, thereby minimizing retrospective biases, and d) collect various sources of information on participants' everyday life. AA approaches have been successfully used to assess a broad range of mental states and psychopathological symptoms in patients and healthy controls. In several studies, AA has shown empirical superiority to retrospective questionnaires by a better prediction of treatment effects or relapses (22, 41).

The context perspective

In any given moment, human emotions, thoughts, and behavior are determined by a complex interaction of genetics, former learning experience and the current environmental context. People act and feel differently if they are alone, together with their partner or in a crowd of people. Similarly, appropriate behaviour differs tremendously between being at work, being at a funeral, having parties during spring break, being at a final exam, etc. Social environment and contextual settings also influence the presentation of clinical disorders. In major depressive disorder (MDD), affective symptoms are related to the time of the day (31). In attention-deficit/hyperactivity disorder (ADHD), patients show enhanced psychopathological

symptoms especially during certain “getting ready” activities (43).

The relation between context and psychopathological symptoms has rarely been studied because traditional assessment approaches, like questionnaires, do not have a within-subject perspective and usually query “beliefs” about people’s own behaviour, instead of multiple context-specific behaviours per subject. AA, however, does offer the possibility to capture context-sensitive information and understand behaviour as being context dependent. Examples of assessed contexts are time of day, social interactions, and location (via GPS). The latter is of special interest because location data enable us to understand behavior in the context of a range of environmental parameters like population density, noise, traffic, etc.

Up to now, AA studies in psychiatry utilizing location data are rare, although as early as 10 years ago, Froehlich and colleagues (17) assessed location via GSM and related it to personal experience. More recent studies assessed whether psychopathological symptoms are related to neighbourhood surroundings in psychiatric disorders, like the work by Epstein et al. (14). Time-stamped location data (via GPS), mood and stress ratings, and drug craving were assessed in 27 poly drug-users who received methadone care due to opioid-dependence. Analyses of the data, comprising 16 consecutive weeks of assessments per participant, showed negative correlations of drug craving, stress and negative mood with the physical condition of the neighbourhood (e.g., including ratings on broken windows, vacant houses, street trash, nonappearance of landscaping, signs of vandalism, etc.). In simpler words, the shabbier the neighbourhood, the less participants craved drugs and experienced stress and negative mood. At first, this result seems to be counterintuitive, and it did not match Epstein et al.’s initial hypothesis. However, in neighbourhoods with low levels of degeneration, drug-users might become aware of the discrepancy between their own health status and the quality of the neighbourhood. Therefore, they might not feel at home in this neighbourhood, which probably makes them feel worse. This study underpins the importance of investigating the effects of location on parameters of mental health.

Gustafson et al. (19) extended this work by including real-time feedback of location data into a clinical intervention. Aiming to improve continuing care for patients suffering from alcohol use disorders, Gustafson et al. (19) equipped 170 alcohol dependent patients with a smartphone application which should improve outcomes of continuing care. The application included several features, such as an audio relaxation guide, a social network assistant, and enlightenment information inspired by cognitive behavioural therapy approaches. Interestingly, Gustafson et al. (19) traced patients’ location and analyzed data in

real-time to provide help when patients approached their favorite bar. Patients using the sophisticated smartphone application during continuing care reported significantly fewer risky drinking days (days on which patients drank more than 4 (men) / 3 (woman) standard drinks within two hours) compared with the control patients not using the app. This study suggests that mental health approaches utilizing location-based feedback may provide useful help during continuing care.

The dynamical perspective

Up to now, most mental health symptoms have been conceptualized as experiencing too much or too little of a regular psychological state (e.g., anxiety, sadness) or as experiencing odd phenomena (e.g., hearing voices). However, emotional experiences, thoughts, behaviours and psychopathological symptoms are dynamic. For instance, affective states wax and wane over time and they are influenced by internal and external factors. Accordingly, internal biological, cognitive factors and external events can modulate affective states from one moment to the next. The relevance of such a dynamic perspective was shown by, e.g., van de Leemput et al. (41), who used temporal autocorrelation and variance of emotions in everyday life to successfully predict upcoming depressive episodes.

The investigation of such dynamic processes is challenging and requires multiple and frequent assessments. Empirical evidence shows that traditional assessment approaches such as retrospective questionnaires are extremely limited in capturing temporal dynamics (34). AA approaches, however, enable researchers to investigate the variability of emotional experiences, thoughts, behaviors and symptoms over time and, moreover, their dynamic interplay with personal experiences and the environment. Fortunately, progress in statistical approaches, namely intensive longitudinal methods (4), now allows for the adequate description of characteristics of dynamic processes. Gathering AA data and utilizing intensive longitudinal methods can result in surprising findings; processes that were initially thought to be stable may show impressive variability over time.

For instance, according to results of traditional assessment strategies, emotions of patients suffering from MDD were assumed to be stable low and/or negative over time. However, AA studies showed impressive affective variability on a day-to-day basis in MDD (5). Even worse, in an e-diary study by Trull et al. (40), it was nearly impossible to see descriptive differences in the ups and downs of the affective states of patients with MDD and patients with borderline personality disorder, although the mood of the first disorder is traditionally described as “unipolar” while the latter disorder is defined as being emotionally un-

stable. Similar results have been reported by Santangelo et al. (32), starting off a discussion of whether affective instability is specifically related to BPD or is a transdiagnostic mechanism.

The real-time perspective

In clinical practice, psychiatrists and psychologists are interested in the evaluation of patients' symptoms to provide the best treatment possible. Retrospective methods (like paper-and-pencil questionnaires) and unstructured clinical interviews are probably the most common assessment strategies used. Here, psychiatrists rely on the ability of a patient to retrospectively assess and reports his or her own symptoms.

However, these tried-and true methods are limited by a number of caveats, including the reliance on the patients' retrospective self-reports, the skill of the clinical interviewer, and the artificial clinical setting of the assessment. Already in 1987, Markgraf et al. (26) showed that nearly all symptoms in patients suffering from panic attacks were retrospectively overestimated; this was most pronounced regarding the "fear of dying". In these questionnaires, patients reported experiencing a "fear of dying" in 70% of all panic attacks. However, using AA to get real-time ratings during real panic attacks revealed that a "fear of dying" was only reported in 3% of all real panic attacks. Since then, retrospective overestimations of symptomatology have been reported multiple times, e.g., in BPD patients who underestimate positive emotions and overestimate negative emotions when they are retrospectively assessed (12).

Basic affective science has revealed a variety of reasons for retrospective biases. Most common are the recency effect, the mood-congruent memory effect and the affective valence effect. Altogether, these effects describe that information is remembered more easily in cases where the information is personally relevant, occurred more recently, is significant or unusual, and is consistent with the current mood at the time of assessment (27, 39). In addition, positive episodes are remembered more easily in general, with the exception of patients with MDD. Compared with retrospective reports, AA approaches bypass all these methodological problems. The FDA acknowledged these problems with retrospective assessments and, accordingly, recommended in their guidelines to use real-time ratings for patient-reported outcomes (16).

The real-life perspective

One of the most obvious advantages of EMA approaches is the ability to study symptoms where they actually occur, i.e., in daily life. Problems associated with the artificial setting of assessment are well known in general. In internal

medicine for instance, the so called "white coat effect" is a well-known phenomenon. In the past, many patients were misdiagnosed and therefore received suboptimal treatment because blood pressure levels measured in the hospital did not correspond to those assessed in everyday life. Therefore, the state-of-the-art technique in assessment of blood pressure is blood-pressure monitoring in everyday life. Transferring this example to research in the mental health field suggests that laboratory studies may be biased since the results may not translate to everyday life.

Both laboratory and everyday life approaches have benefits and disadvantages. We view AA and laboratory experiments not as fundamentally opposed alternatives but instead as complementary approaches. AA can address specific research questions that might not be investigated sufficiently using only laboratory or questionnaire studies. On the other hand, laboratory experiments allow concise testing of hypotheses under the most stringent methodical isolation of the phenomena. In particular, combined research strategies can lead us beyond the perennial struggle of internal versus external/ecological validity (45).

Geospatial data

Geoinformatics (GIScience) is an interdisciplinary research field bringing together informatics, geography and geosciences. The field focuses on the development of tools and methods for the acquisition, storage, analyses, modeling and visualization of geospatial data. It can also be associated with spatial databases and Geographical Information Systems (GIS). When mapping the urban environment, methods from GIScience can be applied in order to address the spatial variations of environmental risk factors.

In cities, each pair of geographical coordinates can be parameterized, e.g., by building density, distance to the nearest street, traffic noise (42), air quality, land use, the amount of vegetation and socio-economic data including age and income (3). In a research study, data might be "gathered" by the participants themselves, in that they observe and interpret their surroundings and report it in a diary or questionnaire (8). The environmental and socio-economic data may also be collected beforehand as a part of the project. The link between the environmental risk factors and the status of the participants is then established in a subsequent step. This approach is less affected by subjective perception of the surroundings. Nevertheless, it also requires the pre-processing of heterogeneous data collected from several sources.

Importantly, some environmental risk factors may mainly vary spatially (e.g., land-use and building density) whereas others may vary both in space and time (e.g., traf-

fic noise, air quality, weather). These fundamental characteristics require different approaches in the data collection and processing pipeline. Land use and building cadastre, which are both spatial data of national interest, are usually available from public sources but can be supplemented with data from private sources. Nevertheless, high resolution data are often associated with high costs. Therefore, crowd sourced data may represent a more cost-efficient data source. When using crowd-sourced data, however, it is important to address both the quality and completeness of the data prior to usage (9). The spatial data collected can be pre-processed in a geoinformatic system (GIS). The work includes geo-coding (i.e., giving geographic coordinates to descriptive information), map-matching (i.e., the positioning of geographical coordinates according to map objects, e.g., a road network), homogenization (i.e., following standards and assuring data consistency), modelling and spatial interpolation, dis-(aggregation)/down- and upscaling and quality evaluation.

The need for pre-processing varies between data sets. The original data source might require the most processing, but the resolution is also usually higher. By applying methods for automated feature extraction, one may, for example, extract the quantity of green space from an aerial image. Lawn and trees can be separated from buildings and streets as shown in Figure 1.

When variations across time are to be addressed, continued measurements of the variable of interest are required. Some spatiotemporal data are, to a certain degree, publicly available from national authorities or other institutions at no cost (e.g., weather data). Other parameters are harder to assess. Due to the large spatial and temporal variations it is, for example, difficult to measure traffic noise. Normally, these data are simulated based on models that depend on several assumptions, e.g., the amount of traffic during daytime, speed limits, noise-blocking objects, etc. The simulation results can be static maps for the day and

night. However, as the temporal variations are not accounted for in more detail, their usefulness when addressing, e.g., the relation between traffic noise and stress is likely limited. Furthermore, non-traffic related noises like those from a temporary construction site are not included in the models. Here, a smart-phone based AA would enable the measurement of noise at the same time as the report is being filled. This could be done by incorporating a smart phone app for noise measurements (25, 33). The disadvantage of continuous noise measurements using a smart-phone is the high sensitivity to extraneous noise (e.g., conversations). The difficulty to identify the source of noise like traffic or a construction site has to be solved through post-processing of the captured data.

To assure secure data storage, a spatial database can be set up. In a spatial database, it is possible to not only conduct queries based on environmental attributes but also based on geographical coordinates. For example, if a person's location is known (as measured with a GPS unit), one may conduct a spatial data base query in real-time and obtain the environmental data associated with this position. This a priori knowledge can also be incorporated in an AA sampling scheme, e.g., to trigger an e-diary entry at locations with certain environmental attributes (10). Such a trigger framework might be set up by using a PostgreSQL database with a PostGIS extension. The web framework Django can thereafter be used for communication between the smartphones and the spatial database on the server (36).



Figure 1

In an urban area, lawn and trees can be extracted from an aerial image. Here on a resolution of 20 cm (orthophoto © GeoBasis-DE/LVermGeoRP2015-07-06).

Triggered e-diaries as an innovative methodological approach to combine the dynamical and context perspectives in psychopathological research

As AA captures symptoms repeatedly over time, defining a time-based design is necessary. This means that the number and frequency of assessment points have to be defined. Whereas several parameters like location and physical activity can be captured continuously using a high sampling frequency (e.g., assessing GPS-data once a second), other parameters, like self-report ratings assessed through an e-diary have to be prompted at certain time points. The most common time-based designs are time-based schedules, event-based schedules and a combination of both, called mixed schedules. Whereas time-based sampling schemes prompt data queries according to a fixed time schedule (e.g., every hour from 8 a.m. to 10 p.m.) or randomly within a certain time frame, event-based sampling methods ask participants to answer questions when predefined events occur (e.g., a drinking episode). Unfortunately, investigating infrequent phenomena or contextual variables in everyday life is challenging.

To investigate associations between mental health variables (like stress) and environmental phenomena (like noise in cities), the assessment of both variables has to be temporally linked. However, both time- and event-based sampling schema are likely to miss rare phenomena of interest. In practice, if a participant moves into the city center for meals every day from 12:15 p.m. to 12:45 p.m., a time-based sampling querying at 12:00 p.m. and 13:00 p.m. will miss assessing the participant's mental states in the city. Other examples include the scenarios of

walking through a park, being temporarily stuck in a traffic jam, etc. From a statistical point of view, correlation coefficients need variance for both parameters, or more simply, if we do not capture "having meal in city center," we are not able to model its effects on mental health. So, to follow our example, a minimal amount of participant ratings during environmental contexts of interest are required.

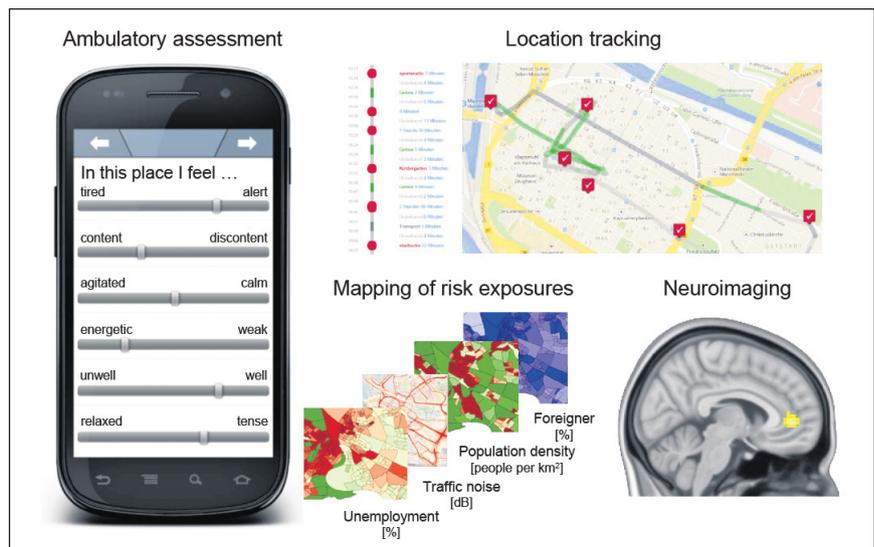
Interactive ambulatory assessment (IAA) can be used to overcome methodological limitations caused by different time courses of the parameters of interest. The aim of IAA is to heighten the amount of e-diary assessments during rare events, like walking through a park. Accordingly, parameters of interest (e.g., location, physical activity, heart rate) are monitored continuously and analyzed in real-time. Once an intended event (like a certain location, a high physical activity episode, a high heart rate, etc.) occurs, the e-diary is triggered to assess the corresponding psychological variables of interest.

Myrtek (30) was the first researcher to use IAA. He investigated whether emotions are associated with physiological processes (additional heart rate). Ebner-Priemer et al. (11) developed an interactive algorithm for the investigation of associations between physical activity and affective states in everyday life. Interestingly, their approach quadrupled the amount of e-diary prompts associated with high physical activity in comparison with a random time-based sampling schema.

Such IAA approaches can be applied to the investigation of associations between environmental components and mental variables, too. Therefore, location parameters are assessed continuously and analyzed in real-time. As soon as an environmental parameter of interest changes, participants are queried regarding their mental

Figure 2

GPS-triggered e-diaries on smartphones (MovisensXS platform, <https://xs.movisens.com>) to trace participants', thereby assessing both momentary mental states and exposure to environmental risk and resilience factors, are combined with neuroimaging data in the PEZ study at the Central Institute of Mental Health in Mannheim, Germany. Graphs are adapted from Nature Neuroscience (37) and reprinted with permission from Heike Tost, Frances A. Champagne and Andreas Meyer-Lindenberg. Map sources: GeoBasis-DE/BKG, Google (location tracking); OpenStreetMap contributors and City of Mannheim Office of City Planning (traffic noise); Nexiga LOCAL (unemployment percentage, population density and foreigner percentage).



states. So, for instance, if a participant moves from the city to a forest, he is requested to rate mood. We call this approach location-based GPS-triggered e-diary (Figure 2).

Using such GPS-triggered e-diaries, Dorn et al. (10) compared a solely time-based trigger algorithm to a trigger algorithm which incorporated land use to optimize the assessment strategy. This trigger enhanced the amount of unique trigger locations and increased the number of triggers at not often visited land uses. Törnros et al. (36) extended Dorn et al.'s work using location data captured in a sample of 143 participants over one week. Their comparison of 4 different sampling methods (two location-, one distance- and one time-based scheme) revealed advantages of location-based sampling strategies. Although the location-based sampling schemes were triggered less often, they enhanced the spatial spread and the e-diary assessments at unique locations and rarely-visited land use types.

PEZ – An ongoing study

GPS-triggered e-diaries are used in an ongoing study at the psycho-epidemiological center, called “Psychoepidemiologisches Zentrum (PEZ)”, of the Central Institute of Mental Health (CIMH) in Mannheim, Germany. This study comprises six work packages, which operate synergistically to identify relevant health-related environmental risks and resilience factors in adolescents and young people. The primary aim of PEZ is to deepen our knowledge of the vulnerability-stress model, i.e., to explore the interaction of individual risk and resilience factors during critical periods of brain development which may predispose individuals to severe psychiatric disorders like schizophrenia, likely via the induction of chronic social stress. The hypothesis considers that the effects of the interaction of environmental factors, like urban stress, and individual risk and resilience factors, like genetic or epigenetic factors, converge on shared neuronal mechanisms, i.e., the sensitization of neural stress regulatory circuits by structural and functional changes in the perigenual anterior cingulate cortex (pACC) (1, 2, 20, 21, 28, 37). Within this vulnerable system, the exposure to social stress later in life is believed to prompt an acute dysregulation of downstream effector sites mediating emotion and stress responses, which can facilitate the development of psychopathological symptoms in adulthood.

To investigate these mechanisms, PEZ promotes the development and validation of innovative methods like GPS-triggered e-diaries combined with functional magnetic resonance imaging (fMRI) and extraction of tissue samples to analyze biomarkers like stress hormones and methylation patterns (see Fig. 2).

The construction of the PEZ sample is based on an accelerated longitudinal design (also called cross-sequential design). The idea of this longitudinal design is the initiation of multiple overlapping single cohorts at the same time with each cohort starting at a different age. The advantages of this design are obvious: a) it considers age-, cohort- and period-effects concurrently; b) the complete age range of interest can be explored in a short period of time; c) missing data through dropout in one cohort could be filled by immediately following cohorts (18). Currently, nine different cohorts with a total age range of prenatal life up to 27 years of age are examined within PEZ. The participants are randomly drawn from local population registers of communities of the Rhine-Neckar region and the cities of Mannheim, Ludwigshafen and Heidelberg, often referred to as “Metropolitan Region Rhine-Neckar”. The selection process is a two stage proportionally layered procedure considering specific stratifications like region (e.g., urban and rural areas), age, gender and ethnic background.

Each follow-up examination chart comprises two appointed days at the study center. The appointed days are eight days apart from each other because participants are requested to wear the GPS-triggered e-diaries for 7 days in their everyday life. On the first appointed day, all participants are clinically characterized by an interview and questionnaire regarding sociodemographic information and personality traits. Furthermore, the AA is issued to the participants. On the second appointed day, the participants return the AA and are requested to give tissue samples. Additionally, a subsample of the participants undergoes an MRI examination consisting of sequences allowing for the quantification of brain structure and brain function during cognitive and emotional tasks.

Implications and outlook

Psychiatric research and its diagnostic methods have been criticized by relying too much upon self-reported signs and symptoms, the lack of a correspondence between these assessments and neurobiological and behavioural systems, the tremendous overlap between diagnoses, and the neglect of fluctuations in disease states (7). Among others, these caveats may plausibly relate to the known difficulties in developing more efficient behavioural and psychopharmacological treatments. Although this is a plausible point of view, we would like to emphasize that considerable optimism is justified.

Psychiatric research is offered an amazing plurality of technologies to study mental health symptoms on a biological and on a self-report level, in the laboratory and in everyday life. With these new technologies, we are able to

track environmental and social stressors in everyday life and relate them to their neurobiological underpinnings. By using longitudinal designs, long term exposure to environmental and social stressors can be related to long term alterations of neurobiological functioning and to the development of mental disorders. Altogether, these methods and methodologies are able to investigate how the interaction of environmental factors (like urban stress generated by population density) and individual risk- and resilience factors (like genetic or epigenetic factors) converge on shared neuronal mechanisms, i.e. the sensitization of neural stress regulatory circuits caused by changes in the perigenual anterior cingulate cortex (pACC) (20), thereby influencing the risk of mental disorders in adulthood. From this perspective, psychiatric research may be just at the beginning of identifying the complex interplay of biological and environmental factors that is at the core of established vulnerability-stress models. This may result not only in much needed novel behavioural and psychopharmacological treatments but also in future guidelines for urban planning that aim at reducing the risk of mental disorders.

Conflict of interest

Markus Reichert, Tobias Törnros, Andreas Hoell, Helen Dorn, Heike Tost, Hans-Joachim Salize, Andreas Meyer-Lindenberg, Alexander Zipf and Ulrich Ebner-Priemer declare that they have no conflicts of interests.

Compliance with ethical guidelines

This article contains no studies on humans or animals.

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