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The List of Competences of Clinical Psychologists as a Professional Asset

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The EACLIPT task force on "Competences of Clinical Psychologists" (this issue; EACLIPT, 2019) has proposed a list of core competences of European clinical psychologists. The document is a discussion paper that outlines a competence profile that covers both, professional knowledge as well as clinical skills. The list of criteria is not considered final, is open to discussion, and shall be updated regularly in interaction with changing environments, new scientific evidence as well as national and/or cultural specificities.

The list extends existing lists of competences (e.g., by the University College of London, n.d.) by not only defining the competences of psychotherapists as a major subgroup of clinical psychologists, but also listing e.g. diagnostic and methodological competences. Thereby, the list covers a wider and more comprehensive range of knowledge and skills of clinical psychologists. Importantly, the task force refrained from defining competences of clinical psychologists in reference to overarching theoretical models or schools. By that, clinical psychologists' competences as well as the quality of their services are defined and may be evaluated regardless of potentially underlying theoretical orientation.

With the presented list, the task force provides an important service to patients and families, to the profession of clinical psychologists as a whole, to society, to educational institutions and students/trainees, as well as to research.

For patients and their families, the list of competencies transparently defines what patients can expect to receive from professionals justifiably calling themselves "clinical psychologist." Thereby, the list may assist potential "customers" and/or patients to navigate through the "psycho-jungle" in search of help for psychological problems and may enable patients to better distinguish between good and not-so-good services. Relatedly, the list

may also help pinpointing potential malpractice by incompetent, wrong, or fraudulent practice of clinical psychologists.

For clinical psychologists as a profession, the list may help to define themselves as a psychology profession, to support the development of a professional identity, as well as to unite clinical psychologists as a group in political and/or professional struggles within respective health care systems. The list may also facilitate communication and cooperation with health care providers of other professions as well as their societies. Depending on the respective national health care system, the list of competences may also help clinical psychologists to receive reimbursement by health insurances. An internationally agreed-upon list of competences of clinical psychologists will foster clinicians' mobility across Europe by defining standard criteria of clinical psychologists' expertise and thereby facilitate accreditation of professional titles by foreign health care systems. A European definition of competences will also facilitate international professional exchange and collaboration within Europe and beyond.

As Strauß and Kohl (2009) have shown for the subgroup of psychotherapists, the conditions of training and practice of clinical psychologists in Europe greatly vary depending on the respective national health care system and can be expected to vary even more if not only psychotherapists are considered. Having an agreed-upon list of competences of clinical psychologists in Europe will surely make professional life easier for practising clinical psychologists as well as health administrators. In case the title of "clinical psychologist" is not yet legally protected and regulated in a particular European country, the list of competences will help to develop legislation related to mental health services in general and clinical psychology in specific. As part of this, the list may also help to develop and refine quality criteria as well as ethical standards and thereby strengthen the trust in clinical psychologists as a profession.

For educational institutions offering teaching and training of future clinical psychologists, the list of competences helps to specify the knowledge and skills that students and trainees should attain to receive an academic degree and/or professional title. However, the question which knowledge and which skills should be taught/trained at which level (Bachelor, master, postgraduate training) and by which institution(s) will have to be answered by specialists within a respective national educational and health care system in coordination with respective authorities.

Future development of potential hierarchies of competences to be sequentially attained may help to develop curricula at different levels of expertise and thereby potentially "streamline" teaching and training in clinical psychology. An according optimization by levels of training may reduce the time and money spent by clinical psychologists in training as well as by the society. Furthermore, the list of competences may not only help to structure curricula, but in turn, practical experiences with implementing the criteria within curricula will inform the continuous refinement, extension and revision of the criteria and the curricula.

Research may also profit from the explication of competence criteria by the EACLIPT list. For example, the teaching and training of single skills, such as interpersonal skills, may be evaluated and may lead to scientifically founded recommendations for eventual modifications of training contents and/or procedures. Also, the explication of clinical skills will facilitate research including diverse therapists and will help to identify potential moderators of skill acquisition. Identification of moderators of skill acquisition may aid the individualization of trainings. Furthermore, the explication of clinical skills nicely parallels the systematic differentiation and research of moderators, mechanisms, and processes of change in psychotherapy (Crits-Christoph, Connolly Gibbons, & Mukherjee, 2013; Doss, 2004), which may to be applied for examining the wider range of clinical psychology and may be brought together to advance our theoretical and clinical knowledge.

Like the list of competences itself, the list of beneficiaries and benefits of the EACLIPT list of competences has to be incomplete and can be extended.

Overall, clinical psychologists having acquired competences as defined by the EACLIPT list will have an excellent foundation for their professional practice of clinical psychology in service of fostering the best possible mental health of their patients.

References

Crits-Christoph, P., Connolly Gibbons, M. B., & Mukherjee, D. (2013). Psychotherapy process-outcome research. In M. J. Lambert (Ed.), *Bergin and Garfield's handbook of psychotherapy and behavior change* (6th ed., pp. 298–340). New York, NY, USA: Wiley.

Doss, B. D. (2004). Changing the way we study change in psychotherapy. *Clinical Psychology: Science and Practice, 11*(4), 368-386. https://doi.org/10.1093/clipsy.bph094

EACLIPT Task Force On "Competences of Clinical Psychologists". (2019). Competences of clinical psychologists. *Clinical Psychology in Europe, 1*(2), Article e35551. https://doi.org/10.32872/cpe.v1i2.35551

Strauß, B., & Kohl, S. (2009). Entwicklung der Psychotherapie und der Psychotherapieausbildung in europäischen Ländern [Development of psychotherapy and psychotherapy training in European countries]. *Psychotherapeut, 54*(6), 457-463. https://doi.org/10.1007/s00278-009-0703-5

University College of London. (n.d.). *Competence frameworks.* Retrieved from https://www.ucl.ac.uk/pals/research/clinical-educational-and-health-psychology/research-groups/core/competence-frameworks

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Research Article

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OK Computer? A Time Analysis of Google Searches About Symptoms

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Abstract

Background: Google searches are now a popular way for individuals to seek information about the significance of common symptoms and whether they should seek medical assistance. As analysis of search patterns may help understand the demand for medical care, we examined what times over a 24-hour period and on what days of the week people searched Google for information about common symptoms.

Method: We analysed Google searches for symptoms in the United Kingdom during the week from July 30 to August 5, 2018 using Google Trends. We recorded the time points with the highest search volume for 50 common symptoms relative to other searches, and the day of the week with the highest search peak for each particular symptom.

Results: All of the peak searches for the symptoms we examined occurred during the night between 10pm and 8am. The majority 32/50 (64%) occurred between 3am to 6am with 12/50 (24%) between midnight and 3am. Most symptom searches were more common during the week and lowest during the weekend. Typically, searches for a particular symptom peaked at a similar time each night over the week.

Conclusions: Searches for symptoms are significantly more common during night-time hours, and particularly between 3 and 6am. Symptom searches show relatively stable diurnal and weekly patterns.

Keywords

Google searches, symptoms, health anxiety, internet, time of day

Highlights

- Google searches for health information are common and individuals regularly search for their specific symptoms before deciding whether to seek medical care.
- Searches for common symptoms are significantly more likely to occur, relative to other searches, during the night-time hours and are highest during the working week and lowest at weekends.
- The majority of symptom searches show relatively stable diurnal and weekly patterns.

Experiencing physical symptoms is very common but it is often difficult for individuals to determine whether the symptom is serious and needs medical attention (Pennebaker, 1982; Petrie & Broadbent, 2019). A recent general population survey showed that individuals experience an average of five symptoms in a week, while 23% of the sample reported experiencing 10 or more symptoms (Petrie, Faasse, Crichton, & Grey, 2014). The meaning of symptoms can often be uncertain and individuals have in the past sought advice from family and friends about whether a symptom is a sign of a serious illness (Hartzband & Groopman, 2010). However, Google is now being used as an alternative resource for understanding symptoms, with Google searches frequently used by the public to determine the significance and threat posed by particular symptoms and whether medical assistance should be sought (Jacobs, Amuta, & Jeon, 2017).

Perhaps it is Google's anonymity, accessibility and information availability that has seen health-related searches become the second most searched thematic area amongst all searches (Sullivan, 2016), with searches for symptoms now accounting for approximately 1% of the three billion searches each day (Pinchin, 2016). In patients specifically, a recent survey of those attending an emergency department found that 49% regularly use the internet for health information and 35% had searched for information on their specific symptoms before presenting (Cocco et al., 2018). Patients can also check their symptoms using online symptom checking algorithms that can provide advice about whether to seek medical care (Semigran, Linder, Gidengil, & Mehrotra, 2015).

There has been concern raised that such searches may lead to a baseless increase in health anxiety or "cyberchondria" due to the fact that searches for common symptoms are often linked to rare, serious or fatal illnesses (Filipkowski et al., 2010; North, Ward, Varkey, & Tulledge-Scheitel, 2012; White & Horvitz, 2009). Given the impact that health anxiety has shown in areas such as healthcare utilisation (Barsky, Ettner, Horsky, & Bates, 2001), there is surprisingly little information available on when individuals search for symptoms and how this may relate to utilisation of health care and the demand for out of hours care.

The access to Google search data through Google Trends has enabled research on how often particular search terms are entered relative to the total volume of searches. This data can also be aggregated for different parts of the world or different time periods. Analyses of search terms by Google Trends has been used to estimate the level of influenza illness in a population (Lampos, Miller, Crossan, & Stefansen, 2015), stock market trends (Preis, Moat, & Stanley, 2013), and to investigate sensitive topics like sexual behaviour, where surveys are likely to lead to misleading data (Stephens-Davidowitz, 2017). Analysis of Google Trends for symptom searches can provide aggregated data on precisely when - during the day or the week - people are more likely to be looking for information about their symptoms and thus offer information about the likely demand for non-urgent care. In this study we examined when individuals searched for common symptoms across a 24-hour period and on what days of the week. Based on previous work on the non-urgent demand for emergency department visits in the United Kingdom, which showed that the majority of non-urgent attendance occurs late at night or in the early hours of the morning (O'Keeffe, Mason, Jacques, & Nicholl, 2018), we hypothesized that Google searches about symptoms would follow a similar pattern.

Method

Symptoms

We used a list of 50 common symptoms to investigate the peak search period for each symptom. Forty-seven symptoms were drawn from a previous study investigating the frequency of symptom complaints in a general population sample (Petrie et al., 2014). These included common symptoms such as back pain, fatigue, headache, insomnia and joint pain. We also added three other terms to the list. This included "hangover", due to the frequency of this condition reported in general population studies (Gjerde et al., 2010; Tolstrup, Stephens, & Grønbaek, 2014) and its association with emergency room and primary care visits (Cherpitel & Ye, 2015). As it has often been acknowledged that searching benign symptoms in Google can produce results suggesting cancer or imminent death (North et al., 2012; White & Horvitz, 2009), we included both "cancer" and "death" in the list.

Google Search Data

Google Trends (trends.google.com) is a publicly available online tool that allows people to analyse how often a specific term or phrase has been searched in Google over a specified time period or in a particular geographic region, relative to other searches (Nuti et al., 2014). Google Trends adjusts the data by taking a random sample of searches for a term and computing its popularity relative to the total number of Google searches over

the same period of time. The time point with highest search volume for a term has the value of 100, while a score of 50 indicates half the popularity.

A Google Trends search for the 50 symptoms or conditions of interest in the United Kingdom was conducted. If a symptom phrase contained 'or', as in fever or increased temperature, this was changed to + in the Google Trend search. Symptoms such as back or neck pain became back pain + neck pain. Prior to searching, computer clocks were changed to London time to ensure that the Google Trend results corresponded to the correct time zone. The time period of the search was the week from July 30 to August 5, 2018. We chose this week during the summer period so the data was less likely to be affected by winter colds and flu viruses. As minutes are only available for time periods of 24-hours or less, Wednesday August 1 was taken as the representative day of the week and the time (hours and minutes) that each symptom was searched the most on this day was recorded. The day of the week that had the greatest number of searches for each symptom was also examined. Collecting data over short periods, such as the week used in the present study, has demonstrated strong predictive power and representation of future data. For example, collecting data from one Saturday-Sunday period can forecast economic trends for subsequent months (Choi & Varian, 2012).

The rate of Google searches during the day (6am to midnight) and night were calculated using www.openepi.com and compared using a mid-P exact method. The median number of symptoms searched for on Google during the hours 6am to midnight was compared to the number at night (midnight to 6am) using the Wilcoxon non-parametric method and a Poisson regression model was to determine whether the number of Google searches performed per hour differed. Analyses were performed in SAS (v 9.4, SAS Institute Inc, Cary, NC). The significance level was set at $p < .05$.

Results

We examined the peak time for searches for each of the 50 symptoms and these are illustrated in Figure 1. All of the peak searches for symptoms occur between 10pm and 8am. Only 3 searches for symptoms (cancer, increased appetite and sexual problems) peak before midnight and only 2 (muscle pain and difficulty concentrating) are after 6am. Of the remaining symptom searches, the majority 32/50 (64%) occur between 3am to 6am, while 12/50 (24%) are between midnight and 3pm; these include death at 1.48am. The hour with the most symptom searches is 4-5am with 16 (32%) conducted during this period.

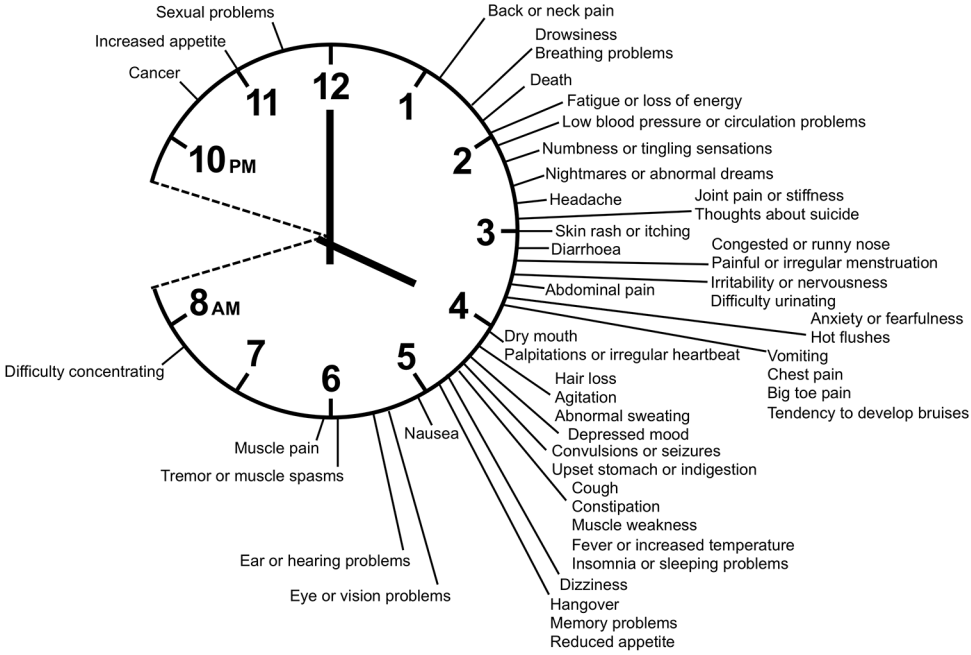

Figure 1. Peak of searches for common symptoms in United Kingdom during the week of July 30 to August 5, 2018.

In total there were 45 symptoms reported in the 6 hours from midnight to 6 am (nighttime) (7.5 searched per hour, 95% CI [5.5, 9.9]). During the day (6am to midnight) there were 5 searches in 18 hours (0.28 searches per hour, 95% CI [.01, 0.62]). There were therefore about 7 searches fewer per hour in the day than at night (rate difference -7.2 (-9.4, -5.0) (mid-P exact comparison of rates ($p < .0001$). Significantly fewer symptoms were reported during the day than at night (median (min, max) 0 (0,2) v 5.5 (0,17) respectively, $p = .001$). There was a significant difference in the number of counts observed between hour blocks (Poisson regression, $p < .0001$).

We next examined the distribution of symptom search peaks over the days of the week we sampled. We found that Monday, Tuesday and Friday had the greatest numbers of peaks of searches for symptoms, each with 10. Saturday was lowest with 3 symptoms, while Wednesday had 7, Thursday 4 and Sunday 6. Most symptoms (76%) did not differ in the peak pattern of searching across the week. This is illustrated in the top two panels of Figure 2, which shows the pattern of searches for cough and vomiting. Death also shows a similar daily pattern. An exception is searches for hangover, which show a strong weekly pattern with higher levels over the weekend and lower numbers of searches for hangover symptoms during the week (bottom of Figure 2).

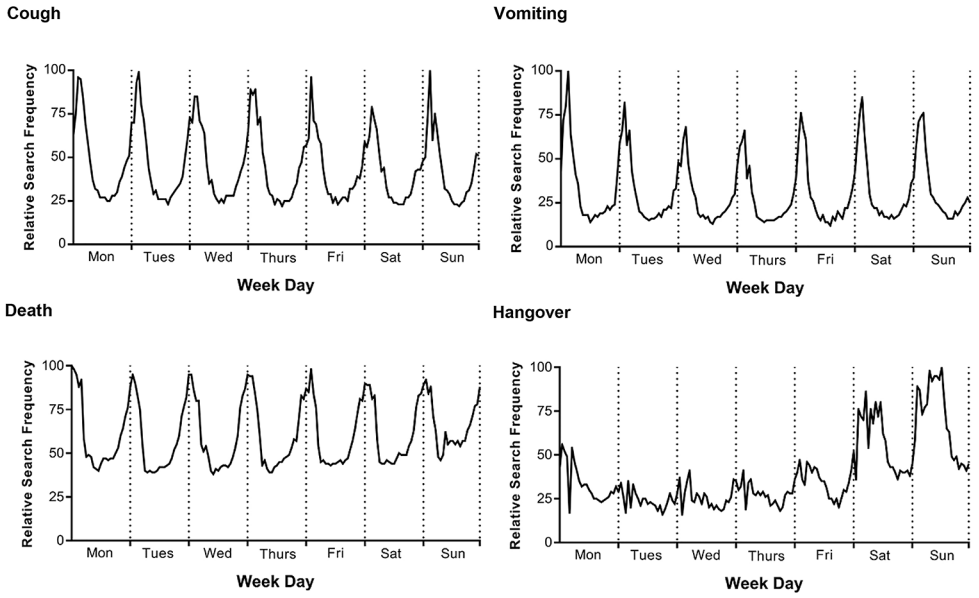

Figure 2. Weekly pattern of symptom searching for cough, vomiting, death and hangover symptoms.

The other symptoms that did not show a strong weekly pattern were increased appetite, sexual problems, low blood pressure, difficulty urinating, muscle weakness, dizziness, bruising easily, agitation, depressed mood, ear or hearing problems and difficulty concentrating.

Discussion

We found searches for symptoms are much more likely to occur relative to other searches during the night-time hours, and particularly between 3 and 6am. Most symptom searches show a consistent pattern over the week, with peaks at similar times of night. Symptom searches are more common during the week and lowest during the weekend. The results suggest that individuals with high levels of health anxiety may be advised to restrict Google symptom searches during the night-time in order to avoid unnecessary worry and healthcare use brought on by anxiety-provoking search results. Another implication may be for clinicians to ask about, and treat, sleeping problems in patients with high levels of somatic complaints.

The pattern of searches for symptoms during the night-time hours is consistent with previous research showing that people are most likely to notice symptoms when they are alone, not distracted by other activity and have time to focus on sensations that they

rarely notice when immersed in daily life (Pennebaker, 1982). The night-time period is also a time when it is difficult to consult medical services about symptom concerns. Previous analysis of Google trends has also noted that searches for the "big" questions such as "What is the meaning of life?" and "Is there life on other planets?" also peak between 2 and 4 am (Stephens-Davidowitz, 2017). The study also highlights the use that can be made of Google Trends for understanding patient search behaviour around health issues. Analysis of Google searches has been used recently for understanding how patients manage their gout and arthritis (Jordan, Pennebaker, Petrie, & Dalbeth, 2018), whether using Google is associated with statin intolerance (Khan, Holbrook, & Shah, 2018) and for seeing if particular internet searches were associated with a subsequent diagnosis of pancreatic cancer (Paparrizos, White, & Horvitz, 2016).

Some limitations of the study should be acknowledged. The data is limited to those with internet access and who use Google as opposed to other search engines. The data is from only one country and needs replication in other locations and in non-English speaking populations. As we used symptoms as specific search terms, we do not know what exactly the search was about or its context. It is also not possible to get absolute rather than relative numbers of searches. It should also be noted that there is a lack of information on how data from Google Trends is derived, including the proportion of total searches sampled and the algorithms involved (Nuti et al., 2014). Bearing these limitations in mind, it is likely that Google Trends may in the future provide more insights into how patients use the internet to seek information on health topics and as a driver for seeking health care.

It is also important to consider that Google searches may have positive effects for patients and healthcare professionals alike. For example, a recent survey of adult patients presenting to an emergency department demonstrated that searching for symptoms on Google and seeking information online resulted in a more positive doctor-patient interaction and did not reduce adherence to treatment (Cocco et al., 2018). For these patients, it may be that the internet serves as a supplementary resource that provides information that supports the doctor's opinions and enhances this relationship (Wald, Dube, & Anthony, 2007). However, this is dependent on the information being searched for reflecting the opinion of the health professional; in cases where the two information sources are incongruent, the relationship can be negatively affected and patients may become more likely to ignore healthcare professional advice (Russ, Giveon, Catarivas, & Yaphe, 2011). As such, while searching for symptoms may have some beneficial outcomes, the extent of this is limited by the accuracy the information searches provide.

This research has various implications for health professionals. Firstly, a greater understanding of patterns of high internet symptom searching may help health professionals better understand and determine the health anxiety levels of a patient, and how that may contribute to the experience of symptoms. Given that patients with higher anxiety levels may be more likely to misattribute general symptoms to an illness (Severeijns,

Vlaeyen, van den Hout, & Picavet, 2004) and are more likely to seek out information about symptoms online (Eastin & Guinsler, 2006), asking about online search activity may be valuable clinical information.

Secondly, this research may have significant applications at a population level such as better management of healthcare services. Recent research has demonstrated that visits to health websites the preceding night can be used to predict emergency department traffic on the following day (Ekström, Kurland, Farrokhnia, Castrén, & Nordberg, 2015). This logic may also be applied to searches for symptoms, where the number of symptoms googled may predict emergency department traffic. Further research should investigate the predictive validity of Google symptom searches, and whether deviations of such from the times and days outlined in the current study have differential implications for healthcare service traffic.

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References

Barsky, A. J., Ettner, S. L., Horsky, J., & Bates, D. W. (2001). Resource utilization of patients with hypochondriacal health anxiety and somatization. *Medical Care, 39*(7), 705-715. https://doi.org/10.1097/00005650-200107000-00007

Cherpitel, C. J., & Ye, Y. (2015). Risky drinking, alcohol use disorders, and health services utilization in the US population: Data from the 2005 and 2010 national alcohol surveys. *Alcoholism: Clinical and Experimental Research, 39*(9), 1698-1704. https://doi.org/10.1111/acer.12801

Choi, H., & Varian, H. (2012). Predicting the present with Google Trends. *The Economic Record, 88*, 2-9. https://doi.org/10.1111/j.1475-4932.2012.00809.x

Cocco, A. M., Zordan, R., Taylor, D. M., Weiland, T. J., Dilley, S. J., Kant, J., . . . Hutton, J. (2018). Dr Google in the ED: Searching for online health information by adult emergency department patients. *The Medical Journal of Australia, 209*(8), 342-347. https://doi.org/10.5694/mja17.00889

Eastin, M. S., & Guinsler, N. M. (2006). Worried and wired: Effects of health anxiety on information-seeking and health care utilization behaviors. *Cyberpsychology & Behavior, 9*(4), 494-498. https://doi.org/10.1089/cpb.2006.9.494

Ekström, A., Kurland, L., Farrokhnia, N., Castrén, M., & Nordberg, M. (2015). Forecasting emergency department visits using internet data. *Annals of Emergency Medicine, 65*(4), 436-442.e1. https://doi.org/10.1016/j.annemergmed.2014.10.008

Filipkowski, K. B., Smyth, J. M., Rutchick, A. M., Santuzzi, A. M., Adya, M., Petrie, K. J., & Kaptein, A. A. (2010). Do healthy people worry? Modern health worries, subjective health complaints,

perceived health, and health care utilization. *International Journal of Behavioral Medicine, 17*(3), 182-188. https://doi.org/10.1007/s12529-009-9058-0

Gjerde, H., Christophersen, A. S., Moan, I. S., Yttredal, B., Walsh, J. M., Normann, P. T., & Mørland, J. (2010). Research use of alcohol and drugs by Norwegian employees: A pilot study using questionnaires and analysis of oral fluid. *Journal of Occupational Medicine and Toxicology, 5*(1), Article 13. https://doi.org/10.1186/1745-6673-5-13

Hartzband, P., & Groopman, J. (2010). Untangling the Web—Patients, doctors, and the Internet. *The New England Journal of Medicine, 362*(12), 1063-1066. https://doi.org/10.1056/NEJMp0911938

Jacobs, W., Amuta, A. O., & Jeon, K. C. (2017). Health information seeking in the digital age: An analysis of health information seeking behavior among US adults. *Cogent Social Sciences, 3*(1), Article 1302785.

Jordan, K. N., Pennebaker, J. W., Petrie, K. J., & Dalbeth, N. (2018). Googling gout: Exploring perceptions about gout through a linguistic analysis of online search activities. *Arthritis Care & Research, 71*, 419-426. https://doi.org/10.1002/acr.23598

Khan, S., Holbrook, A., & Shah, B. R. (2018). Does Googling lead to statin intolerance? *International Journal of Cardiology, 262*, 25-27. https://doi.org/10.1016/j.ijcard.2018.02.085

Lampos, V., Miller, A. C., Crossan, S., & Stefansen, C. (2015). Advances in nowcasting influenza-like illness rates using search query logs. *Scientific Reports, 5*(1), Article 12760. https://doi.org/10.1038/srep12760

North, F., Ward, W. J., Varkey, P., & Tulledge-Scheitel, S. M. (2012). Should you search the internet for information about your acute symptom? *Telemedicine Journal and e-Health, 18*(3), 213-218. https://doi.org/10.1089/tmj.2011.0127

Nuti, S. V., Wayda, B., Ranasinghe, I., Wang, S., Dreyer, R. P., Chen, S. I., & Murugiah, K. (2014). The use of Google Trends in health care research: A systematic review. *PLoS One, 9*(10), Article e109583. https://doi.org/10.1371/journal.pone.0109583

O'Keeffe, C., Mason, S., Jacques, R., & Nicholl, J. (2018). Characterising non-urgent users of the emergency department (ED): A retrospective analysis of routine ED data. *PLoS One, 13*(2), Article e0192855. https://doi.org/10.1371/journal.pone.0192855

Paparrizos, J., White, R. W., & Horvitz, E. (2016). Screening for pancreatic adenocarcinoma using signals from web search logs: Feasibility study and results. *Journal of Oncology Practice / American Society of Clinical Oncology, 12*(8), 737-744. https://doi.org/10.1200/JOP.2015.010504

Pennebaker, J. W. (1982). *The psychology of physical symptoms*. New York, NY, USA: Springer.

Petrie, K. J., & Broadbent, E. (2019). Symptom perception. In C. D. Llewellyn, S. Ayers, C. McManus, S. Newman, K. Petrie, T. Revenson, & J. Weinman (Eds.), *Cambridge handbook of psychology, health and medicine* (3rd ed., pp. 89-92). Cambridge, United Kingdom: Cambridge University Press.

Petrie, K. J., Faasse, K., Crichton, F., & Grey, A. (2014). How common are symptoms? Evidence from a New Zealand national telephone survey. *BMJ Open, 4*(6), Article e005374. https://doi.org/10.1136/bmjopen-2014-005374

Pinchin, V. (2016, June 20). I'm feeling yucky :(Searching for symptoms on Google. *The Keyword.* Retrieved from https://blog.google/products/search/im-feeling-yucky-searching-for-symptoms

Preis, T., Moat, H. S., & Stanley, H. E. (2013). Quantifying trading behavior in financial markets using Google Trends. *Scientific Reports, 3*(1), Article 1684. https://doi.org/10.1038/srep01684

Russ, H., Giveon, S. M., Catarivas, M. G., & Yaphe, J. (2011). The effect of the internet on the patient-doctor relationship from the patient's perspective: A survey from primary care. *The Israel Medical Association Journal, 13*, 220-224.

Semigran, H. L., Linder, J. A., Gidengil, C., & Mehrotra, A. (2015). Evaluations of symptom checkers for self diagnosis and triage: Audit study. *British Medical Journal, 351*, Article h3480. https://doi.org/10.1136/bmj.h3480

Severeijns, R., Vlaeyen, J. W. S., van den Hout, M. A., & Picavet, H. S. J. (2004). Pain catastrophizing is associated with health indices in musculoskeletal pain: A cross-sectional study in the Dutch community. *Health Psychology, 23*(1), 49-57. https://doi.org/10.1037/0278-6133.23.1.49

Stephens-Davidowitz, S. (2017). *Everybody lies.* New York, NY, USA: Harper Collins.

Sullivan, D. (2016, May 24). Google now handles at least 2 trillion searches per year. *Search Engine Land.* Retrieved from http://searchengineland.com/google-nowhandles-2-999-trillion-searches-per-year-250247

Tolstrup, J. S., Stephens, R., & Grønbaek, M. (2014). Does the severity of hangovers decline with age? Survey of the incidence of hangover in different age groups. *Alcoholism, Clinical and Experimental Research, 38*(2), 466-470. https://doi.org/10.1111/acer.12238

Wald, H. S., Dube, C. E., & Anthony, D. C. (2007). Untangling the Web—The impact of Internet use on health care and the physician–patient relationship. *Patient Education and Counseling, 68*(3), 218-224. https://doi.org/10.1016/j.pec.2007.05.016

White, R. W., & Horvitz, E. (2009). Experiences with web search on medical concerns and self diagnosis. *AMIA ... Annual Symposium Proceedings - AMIA Symposium, 2009*, 696-700.

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Scientific Update and Overview

Social Impairments in Mental Disorders: Recent Developments in Studying the Mechanisms of Interactive Behavior

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Abstract

Background: Most mental disorders are associated with impairments in social functioning. Paradigms developed to study social functioning in laboratory settings mostly put participants in a detached observer point of view. However, some phenomena are inherently interactive and studying full-blown reciprocal interactions may be indispensable to understand social deficits in psychopathology.

Method: We conducted a narrative review on recent developments in the field of experimental clinical psychology and clinical social neuroscience that employs a second-person approach to studying social impairments in Autism Spectrum Disorder (ASD), Personality Disorder, Social Anxiety Disorder (SAD), and Schizophrenia.

Results: Recent developments in methodological, analytical, and technical approaches, such as dual eye-tracking, mobile eye-tracking, live video-feed, hyperscanning, or motion capture allow for a more ecologically valid assessment of social functioning. In individuals with ASD, these methods revealed reduced sensitivity to the presence of a real interaction partner as well as diminished behavioral and neural synchronicity with interaction partners. Initial evidence suggests that interactive paradigms might be a powerful tool to reveal reduced interpersonal sensitivity in Personality Disorders and increased interpersonal sensitivity in individuals with SAD.

Conclusion: A shift towards adapting a second-person account has clearly benefitted research on social interaction in psychopathology. Several studies showed profound differences in behavioral and neural measures during actual social interactions, as compared to engaging participants as mere observers. While research using truly interactive paradigms is still in its infancy, it holds great potential for clinical research on social interaction.

Keywords

social interaction, social cognition, second-person approach, mental disorders, social immersion, ecological validity

Highlights

- We review studies adopting a second-person account of social interaction in clinical psychology.
- Studies show profound differences between actual social interactions and mere observations.
- The full extent of impairments in social functioning unfolds only in complex social interactions.
- New methodological developments hold great potential for research on social interaction deficits.

Most mental disorders are associated with impairments in social functioning. Social difficulties are both diagnostic criteria for several disorders such as Autism, Schizophrenia, Social Anxiety Disorder, or Personality Disorders (Kennedy & Adolphs, 2012; Skodol et al., 2002) and also constitute risk factors for developing, sustaining, and exacerbating clinical symptoms (Cacioppo, Hawkley, & Thisted, 2010; Fowler, Allen, Oldham, & Frueh, 2013; Hawkley & Cacioppo, 2010). Though social functioning is complex and challenging to assess, several recent methodological advancements may allow to directly study social-interactive behavior and its underlying (neural) mechanisms in more ecologically valid ways. The goal of this update article is to delineate these developments and their relevance for understanding mental disorders.

Deficits in social functioning can be based on impairments in the underlying social affective and cognitive processes (Amodio & Frith, 2006) that range from basic social attention and memory to empathy and theory of mind (ToM; also termed mentalizing; Happé, Cook, & Bird, 2017; Kanske, 2018). While empathy allows access to other minds via directly sharing other persons' emotional states (de Vignemont & Singer, 2006), mentalizing enables the understanding of others through abstract inference of their thoughts and beliefs (Frith & Frith, 2005). The typical approach to studying these phenomena in experimental clinical psychology and social neuroscience has been criticized as assessing individual minds as detached observers (Fuchs & De Jaegher, 2009). Paradigms ask participants, for instance, to predict the behavior of cartoon characters, classify emotions of static pictures of eyes, or judge the trustworthiness of face photographs. While these tasks have certainly provided valuable insight into the mechanisms of social functioning, they lack the reciprocal nature of full-blown interactions (Bird et al., 2010; Dziobek et al., 2008; Kanske, Böckler, Trautwein, & Singer, 2015; von dem Hagen, Stoyanova, Rowe, Baron-Cohen, & Calder, 2014; Walter et al., 2009).

In contrast to this *observer account* of social cognition, recent developments in philosophy, experimental psychology, and neuroscience call for a *second-person account* that engages participants in real dynamic interactions (e.g., De Jaegher, Di Paolo, & Gallagher, 2010; Gallagher, 2008; Konvalinka & Roepstorff, 2012; Schilbach et al., 2013). Researchers argue that making sense of another person during an embodied and ongoing social interaction occurs implicitly by making use of enactive perception that takes the context of a shared, intersubjective world into account. In real-time social interaction, implicit processes seem to be more relevant than the explicit forms that have been especially emphasized in previous research (Schilbach, 2016). Accordingly, the full extent of deficient social functioning in psychopathology may only manifest in complex social interactions. For instance, autistic individuals report more problems with direct and immediate social interactions than situations involving slow-paced interactions (e.g., email) or social observation.

Recent research has advanced paradigms originating from an observer account of social interaction towards implementing interactions (or at least interactive elements) with one or more real other persons. In addition to examining real, reciprocal interaction, authors suggested that even the potential for reciprocal interaction constitutes an important step forward, as one becomes actively engaged through another person that is experienced as active and salient (Krach, Müller-Pinzler, Westermann, & Paulus, 2013; Risko, Richardson, & Kingstone, 2016) – a process that is also referred to as *social immersion*. Among the novel approaches, research on gaze behavior has taken a leading role. One prominent paradigm makes use of anthropomorphic virtual characters who respond in a contingent way to participants' eye movements, resulting in reciprocal interaction (Wilms et al., 2010). Comparably, Redcay et al. (2010) developed a paradigm using live video-feed that allows for gaze based face-to-face interaction between an experimenter outside and a participant inside a magnetic resonance imaging (MRI) scanner. Yet another setup even enables two participants to interact via live video-feed while simultaneously tracking their eye-movements (Hessels, Cornelissen, Hooge, & Kemner, 2017). Such a dual eye-tracking method has also been implemented in setups wherein two individuals are lying in MRI scanners (e.g., Saito et al., 2010), enabling the simultaneous acquisition of brain activation of two interacting persons (referred to as hyperscanning). Other approaches rely less on technical means but establish real live interaction between participants with, for instance, free eye contact or structured conversations while measuring the allocation of visual attention or indicators of arousal (e.g., Freeth, Foulsham, & Kingstone, 2013; Myllyneva, Ranta, & Hietanen, 2015). While these paradigms sometimes differ substantially in the way they operationalize social interactions, they can be classified along different dimensions, such as complexity of interaction, temporal dynamics, social presence, and embodiment (Table 1).

Table 1

Classification of Studies

Task / Study	Social presence	Interaction complexity	Temporal dynamics	Embodiment	Disorder	Measure
Joint attention (Oberwelland et al., 2017; Redcay et al., 2013; including dual eye-tracking: Bilek et al., 2017; Tanabe et al., 2012)	Yes	Medium low	High	Medium high - visual information	Autism / Borderline Personality Disorder	Neural activity & gaze behavior
Mutual eye-gaze (Hessels et al., 2018; Myllyneva et al., 2015)	Yes	Low	High	Medium high - visual information	Autism / Social Anxiety Disorder	Gaze behavior
Listening to short stories (Rice & Redcay, 2016)	Yes vs. no (experimental condition)	Low	Low	Medium - auditory information	Autism	Neural activity
Listening to short stories (von dem Hagen & Bright, 2017)	Yes vs. no (experimental condition)	No interaction	-	High - visual + auditory information	Autism	Gaze behavior
Live face-to-face interaction (Freeth & Bugembe, 2019; Freeth et al., 2013; Hanley et al., 2015; Hanley et al., 2014; Magrelli et al., 2013; Nadig et al., 2010)	Yes	High	High	Very high - physically present	Autism	Gaze behavior
Live interaction (Fitzpatrick et al., 2017a, 2017b; Romero et al., 2018)	Yes	High	High	Very high - physically present	Autism	Movement kinematics
Performance task, audience present (Chib et al., 2018; Müller-Pinzler et al., 2015)	Yes vs. no (experimental condition)	No interaction	-	Medium high - visual information	Social Anxiety Disorder	Neural activity
Touch anticipation (Scalabrini et al., 2017)	Yes	Low	High	Medium - tactile information	Narcissistic Personality Disorder	Neural activity
Conversation (Takei et al., 2013)	Yes	High	High	Very high - physically present	Schizophrenia	Neural activity

Note. The table summarizes how the reviewed studies (clustered by the kind of task) vary on features of social interaction. These features encompass the social presence of the interaction partner or audience in a mutual social situation; the interaction complexity expresses how much information is transferred during the interaction; the temporal dynamics of the interaction provides information about how quick responses have to be integrated and reacted upon; and the embodiment of the interaction partner expresses how rich s/he is perceived by the participant.

This update article shortly reviews recent laboratory studies that adopt a second-person account of social interaction within clinical experimental psychology and clinical social neuroscience. We want to delineate how novel and ecologically valid measures have hel-

ped to gain new insight into impairments of social interaction, with a particular focus on studies employing advanced experimental and methodological approaches. This kind of research in the context of mental disorders is still scarce and we will focus on Autism Spectrum Disorders, Personality Disorders, Social Anxiety Disorder, and Schizophrenia.

Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a developmental disorder manifested particularly in persistent patterns of deficient social interactive and communicative behavior (e.g., irregular eye contact, behavioral inflexibility in social contexts) (American Psychiatric Association [APA], 2013).

Deficits in joint attention are one of the core impairments in ASD (Dawson, Bernier, & Ring, 2012). Establishing joint attention – for instance, by directing or following another's gaze to an object – is a simple, but inherently interactive process (Redcay, Kleiner, & Saxe, 2012) that can easily be implemented in truly interactive settings. Using a live video-feed, Tanabe and colleagues (2012) employed a dual eye-tracking joint attention task in dyads of ASD and typically developed (TD) participants during MRI hyperscanning. ASD participants showed reduced accuracy at detecting gaze direction, corresponding with reduced neural activation in the left occipital pole, suggesting altered early visual gaze processing. Furthermore, mixed pairs of TD and ASD participants revealed lower neural synchronization in the right inferior frontal gyrus (IFG) than TD-TD pairs, which the authors attributed to problems integrating self- and other-oriented attention in ASD participants. In another joint attention study using a live video-feed, ASD participants did not differ behaviorally from TD participants (Redcay et al., 2013). However, on the neural level, ASD participants (in contrast to TD participants) did not show differential activity between social and non-social conditions in the dorsomedial prefrontal cortex (dmPFC) and left posterior superior temporal sulcus (lpSTS), which might play a role in mutual engagement with a social partner. Similar patterns were observed using virtual interacting avatars (Oberwelland et al., 2017).

Beyond simple joint attention, one study used task-independent dual eye-tracking, instructing participants to look at each other for five minutes (Hessels, Holleman, Cornelissen, Hooge, & Kemner, 2018). Pairs high in autism displayed less two-way eye gaze (i.e., eye contact), but, interestingly, more one-way eye gaze (only one participant looking in the eyes of the other). The interactive nature of this study design could provide support for the so-called *gaze aversion model* (i.e., avoidance of eye contact) over the *gaze indifference model* (i.e., insensitivity to others' eyes) (Moriuchi, Klin, & Jones, 2017).

Directly targeting the role of true interaction, some studies investigated how different degrees of ecological validity differentially influence behavior along autistic traits. Rice and Redcay (2016) implemented a simulated live interaction between participants in an MRI scanner and an experimenter, examining how brain activity is altered depending on

whether participants think speech is addressed to them live versus pre-recorded. Increasing scores in subclinical autism went along with reduced differential dmPFC activation for live compared to pre-recorded speech, presumably reflecting lower perceived liveness of the speaker in high autistic individuals. Similarly, von dem Hagen and Bright (2017) manipulated participants' belief whether the video of a person telling a story was pre-recorded or live. While these different beliefs resulted in modulated attention towards the eye region in low autistic individuals, they did not affect the attention of persons with high autistic traits. Using mobile eye-tracking, Freeth et al. (2013) involved participants in a structured conversation with an experimenter whose social presence varied (live face-to-face interaction versus pre-recorded video). During the pre-recorded video 'interaction', the amount of time looked at the experimenter correlated negatively with subclinical autistic traits, whereas there was no such correlation in the face-to-face interaction. These studies suggest that individuals with ASD display reduced sensitivity to the cues of online versus offline interaction compared to TD individuals.

Several other studies have used mobile eye-tracking in the context of a more natural social environment. During a semi-structured conversation, children with ASD looked less to the face of the experimenter (particularly to the eyes) than children without ASD (Hanley et al., 2014; Magrelli et al., 2013). Children were mostly listening in Hanley and colleagues' (2014) study, and this pattern of reduced looking at their interaction partner's face was not found when children were primarily speaking (Nadig, Lee, Singh, Bosshart, & Ozonoff, 2010). During a structured face-to-face conversation, adults with ASD showed fewer fixations on the eyes and more fixations on the mouth as compared to TD adults, however, they showed no alterations in fixation on the face in general (Hanley et al., 2015). Similarly, Freeth and Bugembe (2019) found no difference in fixations on the face when the social partner's gaze was averted. However, when participants were being looked at directly, individuals with ASD fixated the face for a shorter time than TD individuals. These interactive studies have helped to reveal factors that modulate social attention of autistic individuals, such as conversational phase or gaze direction of the interlocutor.

To capture nonverbal interpersonal behavior beyond eye gaze, several recent studies employed video- or device-based motion tracking (e.g., Fitzpatrick et al., 2017a; Romero et al., 2018). Using a motion-tracking device, Fitzpatrick and colleagues (2017a) implemented a battery of imitation and motor synchronization tasks to capture dynamical measures of synchronicity. Children with ASD showed reduced social synchronization abilities and had difficulties producing consistently timed movements over the course of an interaction. Interestingly, synchronization abilities correlated with performance on a false-belief ToM task (Fitzpatrick et al., 2017b). Romero and colleagues (2018) objectively quantified synchronization of whole-body movement from video recordings of live interactions, showing that complex whole-body synchronicity between children with ASD and clinicians was above chance level, and correlated negatively with ASD severity, that

is, children with higher social-cognitive abilities exhibited more behavioral synchronicity. Such dynamic measures of interpersonal behavior and coordination provide interesting insights into more complex components of social interaction.

In summary, these results underline how ASD research benefits from implementing a second-person approach: Being addressed by a social partner modulates social attention in response to different contextual factors. Depending on the type of paradigm (e.g., joint attention, manipulation of the degree of ecological validity), ASD compared to TD individuals show reduced sensitivity to the presence versus absence of a real-interaction partner, both in neural and in behavioral measures. In addition, ASD participants revealed diminished levels of neural and behavioral synchronicity with TD interaction partners.

Personality Disorders

Personality disorders comprise a number of maladaptive behavioral patterns and cognitive styles (APA, 2013). Based on previous research, we will focus on Borderline Personality Disorder (BPD) and Narcissistic Personality Disorder (NPD).

BPD is characterized by unstable affect and self-image as well as impulsivity, accounting for severely impaired everyday social functioning (APA, 2013). Investigating social interactions through a joint attention task, Bilek and colleagues (2017) assessed live interacting dyads in MRI hyperscanning. Neural coupling at the site of right temporo-parietal junction (rTPJ), a core region for mentalizing processes, was lowest in BPD-healthy control (HC) dyads, which might be a cause for difficulties in social interactions in everyday life. Interestingly, coupling in dyads of remittent BPD and HC was at the level of HC-HC dyads, suggesting a state specificity or reversibility of low neural coupling in BPD.

NPD is characterized by the need for admiration, a lack of empathy as well as pronounced self-absorbedness. In subclinical narcissism, Scalabrini and colleagues (2017) reported higher scores on narcissistic grandiosity going along with reduced activation in the right anterior insula (rAI) in anticipation of touching a human hand. The rAI is a main structure of the so-called salience network that is assumed to switch attention away from internal towards external stimuli, indicating that narcissists might be less responsive to others and rather remain in self-reflective internal processes.

Taken together, though studies employing truly interactive tasks are still sparse in personality disorders, initial evidence indicates the power of these paradigms in revealing reduced interpersonal sensitivity in the respective populations.

Social Anxiety Disorder

The diagnostic criteria for Social Anxiety Disorder (SAD) include fear in social performance situations and the fear of behaving embarrassingly, leading to avoidance of the respective situations altogether (APA, 2013).

Experimental settings that use socially immersive environments in order to induce the feeling of being observed by others are particularly suitable to study social evaluative threat and embarrassment in SAD populations. In doing so, Müller-Pinzler and colleagues (2015) applied a value estimation task to investigate neural pathways of embarrassment. Participants were led to believe that feedback regarding their performance in the experimental task was shared with three confederates outside the scanner room. When feedback on their performance was made public, participants with higher levels of SAD showed heightened visual attention towards their observers' faces, as well as increased activation in medial prefrontal cortex (mPFC) and the right fusiform face area, possibly indicating increased attention to others and mentalizing about how oneself is perceived by the audience. Similar results were reported for the performance in a motor task under observation (Chib, Adachi, & O'Doherty, 2018).

In a behavioral task using dual eye-tracking, pairs of participants were instructed to look at each other for five minutes (Hessels et al., 2018; see section on autism above). Pairs high in subclinical social anxiety were engaged in more frequent, but shorter one-way eye gaze than low social anxiety pairs. Myllyneva et al. (2015) had a person sitting opposite the participant with an LCD screen in between that could be either transparent or opaque. When the switching between transparent and opaque was computer controlled, both SAD adolescents and controls showed higher arousal to direct gaze than to averted gaze by the other person. However, when participants were forced to initiate the social interaction themselves by controlling when the screen turned transparent/opaque, this difference only remained in individuals with SAD. Hence, self-initiated interaction reduced direct-gaze related arousal in healthy participants, but not in SAD participants.

Overall, these results corroborate clinical descriptions of SAD regarding a higher concern of one's public appearance, resulting in increased neural activation of areas associated with mentalizing and face processing. The possibility to actively initiate contact with an interaction partner could reveal different arousal patterns in response to direct (versus averted) gaze between SAD patients and healthy controls.

Schizophrenia

Schizophrenia (SCZ) is a mental disorder characterized by profound changes in behavior, communication, and cognition, with symptoms including hallucinations, disorganized speech and behavior, and delusions that greatly impair interpersonal functioning (APA, 2013; Tandon et al., 2013).

To investigate neural activation in SCZ during live face-to-face conversation, Takei and colleagues (2013) used functional near infrared spectography (fNIRS) in a sample of SCZ patients and controls to investigate neural patterns during live interaction. Specifically, participants and experimenters spoke for fixed intervals about a previously specified topic. SCZ participants exhibited less appropriate speech, lower production of new topics, and spoke less overall. On a neural level, SCZ participants showed decreased activity in bilateral temporal lobes and right inferior frontal gyrus, co-varying with negative symptoms and disorganization, where the authors suggest a causal role of these brain areas.

While the field of SCZ research is still underrepresented regarding the implementation of truly interactive paradigms, these results show an interesting trend that could not have been revealed in other, less interactive tasks.

Conclusion

A shift towards applying a second-person account has clearly benefitted research on social interaction in psychopathology, with the case of autism taking a prominent role. Several studies showed profound differences in behavioral and neural measures during actual social interactions, as compared to engaging participants as mere observers. This pattern suggests that the full extent and the nature of impairments in social functioning unfolds only in complex social interactions.

Furthermore, many social phenomena are inherently interactive and can therefore only manifest themselves in paradigms implementing real dynamic interactions. The second-person account aims at capturing the underlying mechanisms of these phenomena in their entirety. A few published studies employed hyperscanning with dyads consisting of healthy and psychopathological participants during live interaction, enabling the investigation of co-activation patterns and synchronization of brain activity. However, the possibilities to interact while lying in an MRI scanner are highly restricted and paradigms used in this context are limited in their degree of ecological validity. Likewise, the implementation of paradigms employing more complex social interactions introduces new methodological problems, such as complexity of data and reduced experimental control. Here, economic games offer the chance to study social interactions in a controlled environment but with limited flexibility within the interaction. The use of virtual reality bears potential to regain experimental control as the behavior of a virtual character can be manipulated gradually. Usually, this comes at the price of the participants being aware that they interact not with another human but a virtual agent as has been done in experimental studies addressing Autism and psychotic symptoms (e.g., Forbes, Pan, & Hamilton, 2016; Veling, Pot-Kolder, Counotte, van Os, & van der Gaag, 2016). This problem could, however, be overcome by applying a cover story making participants believe

that they interact with a virtual avatar that is controlled by another human (e.g., Wilms et al., 2010).

Outside the scanner, paradigms with real life face-to-face interaction allow assessing the embodied and implicit nature of interactions. The use of technical means such as mobile eye-tracking or motion capturing devices as well as advanced analytical methods represent an advancement in objective quantification of social interactions. However, it should be noted that although these advanced methods enhance the ecological validity of social interactions in the laboratory, assessing factors like emotions or the dynamics of interpersonal relations remains challenging. Here, field methods and self-report measures are still the means of choice: ecological momentary assessment (EMA) – the collection of various types of data via portable technical devices – has the advantage of capturing real-life social interactions while (or shortly after) they are happening. Furthermore, they can be complemented with more objective measures such as the electronically activated recorder (EAR). Here, participants wear a portable audio recorder that periodically records the acoustic environment, allowing for the analysis of, for instance, the words or prosody used during social interaction or the number of interaction partners.

In conclusion, paradigms employing a second-person approach to the study of social interactions in mental disorders have yielded promising results. While research using truly interactive paradigms is still in its infancy, it holds great potential for clinical research on social interaction.

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References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA, USA: American Psychiatric Publishing.

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: The medial frontal cortex and social cognition. *Nature Reviews Neuroscience, 7*(4), 268-277. https://doi.org/10.1038/nrn1884

Bilek, E., Stößel, G., Schäfer, A., Clement, L., Ruf, M., Robnik, L., . . . Meyer-Lindenberg, A. (2017). State-dependent cross-brain information flow in borderline personality disorder. *JAMA Psychiatry, 74*(9), 949-957. https://doi.org/10.1001/jamapsychiatry.2017.1682

Bird, G., Silani, G., Brindley, R., White, S., Frith, U., & Singer, T. (2010). Empathic brain responses in insula are modulated by levels of alexithymia but not autism. *Brain, 133*(5), 1515-1525. https://doi.org/10.1093/brain/awq060

Cacioppo, J. T., Hawkley, L. C., & Thisted, R. A. (2010). Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychology and Aging, 25*(2), 453-463. https://doi.org/10.1037/a0017216

Chib, V. S., Adachi, R., & O'Doherty, J. P. (2018). Neural substrates of social facilitation effects on incentive-based performance. *Social Cognitive and Affective Neuroscience, 13*(4), 391-403. https://doi.org/10.1093/scan/nsy024

Dawson, G., Bernier, R., & Ring, R. H. (2012). Social attention: A possible early indicator of efficacy in autism clinical trials. *Journal of Neurodevelopmental Disorders, 4*(1), Article 11. https://doi.org/10.1186/1866-1955-4-11

De Jaegher, H., Di Paolo, E., & Gallagher, S. (2010). Can social interaction constitute social cognition? *Trends in Cognitive Sciences, 14*(10), 441-447. https://doi.org/10.1016/j.tics.2010.06.009

de Vignemont, F., & Singer, T. (2006). The empathic brain: How, when and why? *Trends in Cognitive Sciences, 10*(10), 435-441. https://doi.org/10.1016/j.tics.2006.08.008

Dziobek, I., Rogers, K., Fleck, S., Bahnemann, M., Heekeren, H. R., Wolf, O. T., & Convit, A. (2008). Dissociation of cognitive and emotional empathy in adults with Asperger syndrome using the Multifaceted Empathy Test (MET). *Journal of Autism and Developmental Disorders, 38*(3), 464-473. https://doi.org/10.1007/s10803-007-0486-x

Fitzpatrick, P., Romero, V., Amaral, J. L., Duncan, A., Barnard, H., Richardson, M. J., & Schmidt, R. C. (2017a). Evaluating the importance of social motor synchronization and motor skill for understanding autism. *Autism Research, 10*(10), 1687-1699. https://doi.org/10.1002/aur.1808

Fitzpatrick, P., Romero, V., Amaral, J. L., Duncan, A., Barnard, H., Richardson, M. J., & Schmidt, R. C. (2017b). Social motor synchronization: Insights for understanding social behavior in autism. *Journal of Autism and Developmental Disorders, 47*(7), 2092-2107. https://doi.org/10.1007/s10803-017-3124-2

Forbes, P. A. G., Pan, X., & Hamilton, A. F. D. C. (2016). Reduced mimicry to virtual reality avatars in autism spectrum disorder. *Journal of Autism and Developmental Disorders, 46*(12), 3788-3797. https://doi.org/10.1007/s10803-016-2930-2

Fowler, J. C., Allen, J. G., Oldham, J. M., & Frueh, B. C. (2013). Exposure to interpersonal trauma, attachment insecurity, and depression severity. *Journal of Affective Disorders, 149*(1–3), 313-318. https://doi.org/10.1016/j.jad.2013.01.045

Freeth, M., & Bugembe, P. (2019). Social partner gaze direction and conversational phase; factors affecting social attention during face-to-face conversations in autistic adults? *Autism, 23*(2), 503-513. https://doi.org/10.1177/1362361318756786

Freeth, M., Foulsham, T., & Kingstone, A. (2013). What affects social attention? Social presence, eye contact and autistic traits. *PLOS ONE, 8*(1), Article e53286. https://doi.org/10.1371/journal.pone.0053286

Frith, C., & Frith, U. (2005). Theory of mind. *Current Biology, 15*(17), R644-R645. https://doi.org/10.1016/j.cub.2005.08.041

Fuchs, T., & De Jaegher, H. (2009). Enactive intersubjectivity: Participatory sense-making and mutual incorporation. *Phenomenology and the Cognitive Sciences, 8*(4), 465-486. https://doi.org/10.1007/s11097-009-9136-4

Gallagher, S. (2008). Direct perception in the intersubjective context. *Consciousness and Cognition, 17*(2), 535-543. https://doi.org/10.1016/j.concog.2008.03.003

Hanley, M., Riby, D. M., Carty, C., Melaugh McAteer, A., Kennedy, A., & McPhillips, M. (2015). The use of eye-tracking to explore social difficulties in cognitively able students with autism spectrum disorder: A pilot investigation. *Autism, 19*(7), 868-873. https://doi.org/10.1177/1362361315580767

Hanley, M., Riby, D. M., McCormack, T., Carty, C., Coyle, L., Crozier, N., . . . McPhillips, M. (2014). Attention during social interaction in children with autism: Comparison to specific language impairment, typical development, and links to social cognition. *Research in Autism Spectrum Disorders, 8*(7), 908-924. https://doi.org/10.1016/j.rasd.2014.03.020

Happé, F., Cook, J. L., & Bird, G. (2017). The structure of social cognition: In(ter)dependence of sociocognitive processes. *Annual Review of Psychology, 68*, 243-267. https://doi.org/10.1146/annurev-psych-010416-044046

Hawkley, L. C., & Cacioppo, J. T. (2010). Loneliness matters: A theoretical and empirical review of consequences and mechanisms. *Annals of Behavioral Medicine, 40*(2), 218-227. https://doi.org/10.1007/s12160-010-9210-8

Hessels, R. S., Cornelissen, T. H. W., Hooge, I. T. C., & Kemner, C. (2017). Gaze behavior to faces during dyadic interaction. *Canadian Journal of Experimental Psychology, 71*(3), 226-242. https://doi.org/10.1037/cep0000113

Hessels, R. S., Holleman, G. A., Cornelissen, T. H. W., Hooge, I. T. C., & Kemner, C. (2018). Eye contact takes two – autistic and social anxiety traits predict gaze behavior in dyadic interaction. *Journal of Experimental Psychopathology, 9*(2), 1-17. https://doi.org/10.5127/jep.062917

Kanske, P. (2018). The social mind: Disentangling affective and cognitive routes to understanding others. *Interdisciplinary Science Reviews, 43*(2), 115-124. https://doi.org/10.1080/03080188.2018.1453243

Kanske, P., Böckler, A., Trautwein, F. M., & Singer, T. (2015). Dissecting the social brain: Introducing the EmpaToM to reveal distinct neural networks and brain-behavior relations for empathy and theory of mind. *NeuroImage, 122*, 6-19. https://doi.org/10.1016/j.neuroimage.2015.07.082

Kennedy, D. P., & Adolphs, R. (2012). The social brain in psychiatric and neurological disorders. *Trends in Cognitive Sciences, 16*(11), 559-572. https://doi.org/10.1016/j.tics.2012.09.006

Konvalinka, I., & Roepstorff, A. (2012). The two-brain approach: How can mutually interacting brains teach us something about social interaction? *Frontiers in Human Neuroscience, 6*, Article 215. https://doi.org/10.3389/fnhum.2012.00215

Krach, S., Müller-Pinzler, L., Westermann, S., & Paulus, F. M. (2013). Advancing the neuroscience of social emotions with social immersion. *Behavioral and Brain Sciences, 36*(4), 427-428. https://doi.org/10.1017/S0140525X12001951

Magrelli, S., Jermann, P., Noris, B., Ansermet, F., Hentsch, F., Nadel, J., & Billard, A. (2013). Social orienting of children with autism to facial expressions and speech: A study with a wearable eye-tracker in naturalistic settings. *Frontiers in Psychology, 4*, Article 840. https://doi.org/10.3389/fpsyg.2013.00840

Moriuchi, J. M., Klin, A., & Jones, W. (2017). Mechanisms of diminished attention to eyes in autism. *American Journal of Psychiatry, 174*(1), 26-35. https://doi.org/10.1176/appi.ajp.2016.15091222

Müller-Pinzler, L., Gazzola, V., Keysers, C., Sommer, J., Jansen, A., Frässle, S., . . . Krach, S. (2015). Neural pathways of embarrassment and their modulation by social anxiety. *NeuroImage, 119*, 252-261. https://doi.org/10.1016/j.neuroimage.2015.06.036

Myllyneva, A., Ranta, K., & Hietanen, J. K. (2015). Psychophysiological responses to eye contact in adolescents with social anxiety disorder. *Biological Psychology, 109*, 151-158. https://doi.org/10.1016/j.biopsycho.2015.05.005

Nadig, A., Lee, I., Singh, L., Bosshart, K., & Ozonoff, S. (2010). How does the topic of conversation affect verbal exchange and eye gaze? A comparison between typical development and high-functioning autism. *Neuropsychologia, 48*(9), 2730-2739. https://doi.org/10.1016/j.neuropsychologia.2010.05.020

Oberwelland, E., Schilbach, L., Barisic, I., Krall, S. C., Vogeley, K., Fink, G. R., . . . Schulte-Rüther, M. (2017). Young adolescents with autism show abnormal joint attention network: A gaze contingent fMRI study. *NeuroImage: Clinical, 14*, 112-121. https://doi.org/10.1016/j.nicl.2017.01.006

Redcay, E., Dodell-Feder, D., Mavros, P. L., Kleiner, M., Pearrow, M. J., Triantafyllou, C., . . . Saxe, R. (2013). Atypical brain activation patterns during a face-to-face joint attention game in adults with autism spectrum disorder. *Human Brain Mapping, 34*(10), 2511-2523. https://doi.org/10.1002/hbm.22086

Redcay, E., Dodell-Feder, D., Pearrow, M. J., Mavros, P. L., Kleiner, M., Gabrieli, J. D. E., & Saxe, R. (2010). Live face-to-face interaction during fMRI: A new tool for social cognitive neuroscience. *NeuroImage, 50*(4), 1639-1647. https://doi.org/10.1016/j.neuroimage.2010.01.052

Redcay, E., Kleiner, M., & Saxe, R. (2012). Look at this: The neural correlates of initiating and responding to bids for joint attention. *Frontiers in Human Neuroscience, 6*, Article 169. https://doi.org/10.3389/fnhum.2012.00169

Rice, K., & Redcay, E. (2016). Interaction matters: A perceived social partner alters the neural processing of human speech. *NeuroImage, 129*, 480-488. https://doi.org/10.1016/j.neuroimage.2015.11.041

Risko, E. F., Richardson, D. C., & Kingstone, A. (2016). Breaking the fourth wall of cognitive science: Real-world social attention and the dual function of gaze. *Current Directions in Psychological Science, 25*(1), 70-74. https://doi.org/10.1177/0963721415617806

Romero, V., Fitzpatrick, P., Roulier, S., Duncan, A., Richardson, M. J., & Schmidt, R. C. (2018). Evidence of embodied social competence during conversation in high functioning children with autism spectrum disorder. *PLOS ONE, 13*(3), Article e0193906. https://doi.org/10.1371/journal.pone.0193906

Saito, D. N., Tanabe, H. C., Izuma, K., Hayashi, M. J., Morito, Y., Komeda, H., . . . Sadato, N. (2010). "Stay Tuned": Inter-individual neural synchronization during mutual gaze and joint attention. *Frontiers in Integrative Neuroscience, 4*, Article 127. https://doi.org/10.3389/fnint.2010.00127

Scalabrini, A., Huang, Z., Mucci, C., Perrucci, M. G., Ferretti, A., Fossati, A., . . . Ebisch, S. J. H. (2017). How spontaneous brain activity and narcissistic features shape social interaction. *Scientific Reports, 7*(1), Article 9986. https://doi.org/10.1038/s41598-017-10389-9

Schilbach, L. (2016). Towards a second-person neuropsychiatry. *Philosophical Transactions of the Royal Society of London: Series B. Biological Sciences, 371*, Article 20150081. https://doi.org/10.1098/rstb.2015.0081

Schilbach, L., Timmermans, B., Reddy, V., Costall, A., Bente, G., Schlicht, T., & Vogeley, K. (2013). Toward a second-person neuroscience. *Behavioral and Brain Sciences, 36*(4), 393-414. https://doi.org/10.1017/S0140525X12000660

Skodol, A. E., Gunderson, J. G., McGlashan, T. H., Dyck, I. R., Stout, R. L., Bender, D. S., . . . Oldham, J. M. (2002). Functional impairment in patients with schizotypal, borderline, avoidant, or obsessive-compulsive personality disorder. *American Journal of Psychiatry, 159*(2), 276-283. https://doi.org/10.1176/appi.ajp.159.2.276

Takei, Y., Suda, M., Aoyama, Y., Yamaguchi, M., Sakurai, N., Narita, K., . . . Mikuni, M. (2013). Temporal lobe and inferior frontal gyrus dysfunction in patients with schizophrenia during face-to-face conversation: A near-infrared spectroscopy study. *Journal of Psychiatric Research, 47*(11), 1581-1589. https://doi.org/10.1016/j.jpsychires.2013.07.029

Tanabe, H. C., Kosaka, H., Saito, D. N., Koike, T., Hayashi, M. J., Izuma, K., . . . Sadato, N. (2012). Hard to "tune in": Neural mechanisms of live face-to-face interaction with high-functioning autistic spectrum disorder. *Frontiers in Human Neuroscience, 6*, Article 268. https://doi.org/10.3389/fnhum.2012.00268

Tandon, R., Gaebel, W., Barch, D. M., Bustillo, J., Gur, R. E., Heckers, S., . . . Carpenter, W. (2013). Definition and description of schizophrenia in the DSM-5. *Schizophrenia Research, 150*(1), 3-10. https://doi.org/10.1016/j.schres.2013.05.028

Veling, W., Pot-Kolder, R., Counotte, J., van Os, J., & van der Gaag, M. (2016). Environmental social stress, paranoia and psychosis liability: A virtual reality study. *Schizophrenia Bulletin, 42*(6), 1363-1371. https://doi.org/10.1093/schbul/sbw031

von dem Hagen, E. A. H., & Bright, N. (2017). High autistic trait individuals do not modulate gaze behaviour in response to social presence but look away more when actively engaged in an interaction. *Autism Research, 10*(2), 359-368. https://doi.org/10.1002/aur.1666

von dem Hagen, E. A. H., Stoyanova, R. S., Rowe, J. B., Baron-Cohen, S., & Calder, A. J. (2014). Direct gaze elicits atypical activation of the theory-of-mind network in autism spectrum conditions. *Cerebral Cortex, 24*(6), 1485-1492. https://doi.org/10.1093/cercor/bht003

Walter, H., Ciaramidaro, A., Adenzato, M., Vasic, N., Ardito, R. B., Erk, S., & Bara, B. G. (2009). Dysfunction of the social brain in schizophrenia is modulated by intention type: An fMRI study. *Social Cognitive and Affective Neuroscience, 4*(2), 166-176. https://doi.org/10.1093/scan/nsn047

Wilms, M., Schilbach, L., Pfeiffer, U., Bente, G., Fink, G. R., & Vogeley, K. (2010). It's in your eyes-using gaze-contingent stimuli to create truly interactive paradigms for social cognitive and affective neuroscience. *Social Cognitive and Affective Neuroscience, 5*(1), 98-107. https://doi.org/10.1093/scan/nsq024

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Scientific Update and Overview

The Emerging Role of Clinical Pharmacopsychology

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Abstract

Background: Clinical pharmacopsychology is an area of clinical psychology that is concerned with the application of clinimetric methods to the assessment of psychotropic effects of drugs on psychological functioning, and the interaction of such drugs with specific or non-specific treatment ingredients. Clinical pharmacopsychology derives its data from observational and controlled studies on clinical populations and refers to the therapeutic use of medical drugs, not to the effects of substances used for other purposes.
Method: Domains and operational settings of clinical pharmacopsychology are illustrated.
Results: The domains of clinical pharmacopsychology extend over several areas of application which encompass the psychological effects of psychotropic drugs (with particular emphasis on subclinical changes), the characteristics that predict responsiveness to treatment, the vulnerabilities induced by treatment (i.e., side effects, behavioral toxicity, iatrogenic comorbidity), and the interactions between drug therapy and psychological variables. A service for clinical pharmacopsychology is here proposed as an example of the innovative role of clinical psychology in medical settings.
Conclusion: Clinical pharmacopsychology offers a unifying framework for the understanding of clinical phenomena in medical and psychiatric settings. Its aim is to provide a comprehensive assessment of the clinical important changes that are concerned with wanted and expected treatment effects; treatment-induced unwanted side effects; and the patient's own personal experience of a change in terms of well-being and/or quality of life. It is now time to practice clinical pharmacopsychology, creating ad hoc services in Europe.

Keywords

clinical pharmacopsychology, antidepressant drugs, psychotropic medication, clinical service, psychopharmacology

Highlights

- Clinical pharmacopsychology assesses the effects of medications on psychological functioning
- Since clinical psychologists visit medicated patients, a comprehensive clinical evaluation is crucial
- Vulnerabilities induced by psychotropic drugs are an important area of application of clinical pharmacopsychology

The term "pharmacopsychology" was introduced by Kraepelin to indicate the effects of medical drugs on psychological functioning (Kraepelin, 1892). He thought it was important to describe the psychological changes induced by pharmacotherapy. Later, Pierre Pichot edited a volume of psychological measurements in psychopharmacology (Pichot, 1974) outlining new needs that derived from measuring the changes induced by psychotropic medications. Two categories of instruments were collected by Pichot (Pichot, 1974) for psychometric measurement in psychopharmacology: self-rating instruments (e.g., the Hopkins Symptom Checklist - HSCL) (Derogatis, Lipman, Rickels, Uhlenmuth, & Covi, 1974) and clinician-reported rating scales (e.g., the Hamilton Depression Scale) (Hamilton, 1974). Over time, experimental pharmacopsychology was also defined, thus contributing to differentiate pharmacopsychology from psychopharmacology and introducing psychology into the clinical and psychiatric field (Eysenck, 1963; Janke, 1983; Janke, Debus, & Erdmann, 2000; Janke & Netter, 2004; Lipton, Di Mascio, & Killam, 1977).

The term "clinical pharmacopsychology" has been introduced to indicate the clinical psychology approach to pharmacology (Fava, Tomba, & Bech, 2017). Clinical pharmacopsychology was defined as the application of clinimetric methods to the assessment of psychotropic effects of medications, and the interaction of drugs with specific and non-specific treatment ingredients (Fava, Tomba, & Bech, 2017). It should be differentiated from the approach of experimental psychology to pharmacology, i.e., experimental pharmacopsychology. Clinical pharmacopsychology derives its data from observational and controlled studies on clinical populations, whereas experimental pharmacopsychology derives its data mainly from the laboratory and does not necessarily involve clinical populations. Clinical pharmacopsychology refers to the therapeutic use of medical drugs and should be differentiated from the study of the effects of substances used for other purposes (Fava, Tomba, & Bech, 2017).

In experimental psychology the distinction between pharmacopsychology and psychopharmacology is very clear. Pharmacopsychology is defined as the use of drugs as tools to discover or explain psychological functions or to detect differences in drug responsiveness, mostly in healthy persons serving as models for psychiatric diseases (Eysenck, 1963; Janke, 1983; Janke, Debus, & Erdmann, 2000) while psychopharmacology

is defined as the discipline investigating psychological effects of drugs usually in clinical groups; it also includes treatment prediction, drug responsiveness and side effects, always in the context of clinical investigations (Lipton, Di Mascio, & Killam, 1977).

An essential characteristic of clinical pharmacopsychology is that it refers to a clinimetric, instead of a psychometric, conceptual model. Clinimetrics has a set of rules which governs the structure of indices, the choice of component variables, the evaluation of consistency and validity, and differs from classical psychometrics (Bech, 2016; Fava, Tomba, & Sonino, 2012; Feinstein, 1987). An essential clinimetric requisite for an assessment method is its discrimination properties (i.e., responsiveness/sensitivity), which means that the tool should be able to detect clinically relevant changes in health status over time (Fava, Tomba, & Bech, 2017). Just as important is incremental validity which refers to the unique contribution (or incremental increase) in predictive power associated with a particular assessment procedure in the clinical decision process (Fava, Rafanelli, & Tomba, 2012).

We will here describe the most important domains which pertain to clinical pharmacopsychology and propose a setting for clinical pharmacopsychology.

Domains of Clinical Pharmacopsychology

The domains of clinical pharmacopsychology extend over several areas of application which encompass the psychological effects of psychotropic drugs, the characteristics that predict responsiveness to treatment, the vulnerabilities induced by treatment (i.e., side effects, behavioral toxicity, iatrogenic comorbidity), and the interactions between drug therapy and psychological variables.

Psychological Effects of Psychotropic Drugs

In 1968, DiMascio and Shader criticized the tendency "to select, from among the many pharmacologic actions that a drug may possess, a specific effect to consider as the main (therapeutic or beneficial) effect and to describe all others as side-effects" (DiMascio & Shader, 1968, p. 617). They noted that a drug effect such as sedation or motor stimulation may be considered adverse for one patient, and yet therapeutic and desired for another one. Similarly, within the same patient it may be of value at one stage of an illness and adverse at a later stage.

In clinical trials, a limited number of symptoms is usually selected to test efficacy and psychological measurements are targeted. These pragmatic needs have limitations since excessive reliance on symptoms that are part of diagnostic criteria of mental disorders (e.g., major depressive disorder and generalized anxiety disorder) has impoverished clinical assessment.

Indices may be observer-rated or self-rated. While observer-rated methods make full use of the clinical experience and comparison potential of the interviewer, self-rating methods allow a more direct assessment of the patient's subjective perceptions. For instance, when the aim is to assess quality of life, research in this area seeks essentially two kinds of information: the functional status of the individual and the patient's appraisal of their own health. Indeed, the subjective perception of health status (e.g., lack of well-being, demoralization, difficulties fulfilling personal and family responsibilities) is as valid as that of the clinician in evaluating outcomes (Bech, 1990; Topp, Østergaard, Søndergaard, & Bech, 2015). The emphasis on patient-reported outcomes, any report coming directly from patients about how they function or feel in relation to a health condition or its therapy (Clancy & Collins, 2010), is in line with this conceptualization.

An interesting example of standard assessment of psychological effects of antidepressant drugs can be found in placebo-controlled studies which observed that antidepressants decrease reactivity to social environment in depressed patients as assessed by the Clinical Interview for Depression (Guidi, Fava, Bech, & Paykel, 2011). The decrease may certainly be beneficial in an acute depressive state. However, it is conceivable, even though yet to be adequately investigated, that in a residual phase the same effect may entail apathy (Rothschild, Raskin, Wang, Marangell, & Fava, 2014). To ascertain this, however, one needs to rate reactivity to environmental stimuli and apathy, something that is omitted in standard clinical trials (Guidi et al., 2011; Rothschild et al., 2014). Further, high sensitivity is required for detecting residual symptomatology, which was found to characterize most of the patients who were judged to be remitted according to the DSM criteria and no longer in need of active treatment (Fava, Rafanelli, & Tomba, 2012). Excessive reliance on symptoms that are part of diagnostic criteria of mental disorders (e.g., major depressive disorder, generalized anxiety disorder) does not reflect the broad spectrum of variables that affect clinical presentations: subclinical distress (Fava, Rafanelli, & Tomba, 2012), such as demoralization and irritable mood (Fava, Cosci, & Sonino, 2017), psychological well-being and euthymia (Fava & Bech, 2016), mental pain (de Leon, Baca-Garcia, & Blasco-Fontecilla, 2015; Verrocchio et al., 2016), social adjustment (Bech, 2005) and neuroticism (Tyrer, Tyrer, & Guo, 2016).

Likelihood of Responsiveness

Richardson and Doster (2014) underscored that, in the process of evidence-based decision, one should include: 1. *baseline risk* of poor outcomes from an index disorder without treatment, which is important to identify if the treatment produced benefits; 2. *responsiveness* to the treatment option, which is important to verify if remission has been obtained; 3. *vulnerability* to the adverse effects of treatment, which is important to verify if the treatment triggered an iatrogenic comorbid disorder or if the treatment caused reversible or irreversible side effects.

The likelihood of responsiveness to a certain drug treatment and the clinical characteristics that predict response are a crucial issue in psychopharmacology, even though, in recent years, excessive emphasis on the treatment of the average patient has decreased interest in these aspects (Bech, 2016; Fava, 2017; Richardson & Doster, 2014).

While there is a clinical need to have the broadest picture of the effects of a drug, determination of responsiveness may be based on selected items (Bech, 2016). In addition, it has become common practice in clinical trials to quantify the number of participants who, after a pharmacologic and/or psychotherapeutic trial, achieve response or remission according to specific cut-off points of rating scales (Guidi et al., 2018). Remission can be expressed either as a categorical variable (e.g., present/absent) or as a comparative category (e.g., non-recovered, slightly recovered, moderately recovered, or greatly recovered) which refers to the clinical distance between the current state of the patient and his pretreatment position (Bech, 1990). This method of research has limitations and makes difficult the translation of the research results into practice. For instance, an improvement according to specific cut-off points of rating scales might not mirror a real clinical improvement of the patients as it is perceived by the patient or observed by the clinician.

In the same vein, many studies are concerned with relapse and recurrence as primary outcome measures, even though adequate criteria are not available for all mental health conditions and clinicians and researchers in clinical psychiatry often confuse response to treatment for full recovery (Bech, 1990; Fava, 1996).

Finally, where differentiation according to cogent subgroups is made in clinical trials, a treatment which is helpful on average in the average patient might be ineffective in some patients (i.e., no difference with placebo) and even harmful in someone else (i.e., worse than placebo) (Horwitz, Hayes-Conroy, & Singer, 2017; Horwitz, Singer, Makuch, & Viscoli, 1996).

In this framework, clinimetrics can offer an accurate method to measure responsiveness to a treatment. This method is based on staging an assessment of the longitudinal development and of the longitudinal rollback of mental disorders (Cosci & Fava, 2013). Staging differs from the conventional diagnostic practice in that it does not only define the extent of progression of a disorder at a particular point in time but also where a person is currently along the continuum of the course of illness. Staging defines prodromes (e.g., early symptoms and signs that differ from the acute clinical phase) and residual symptoms (e.g., persistent symptoms and signs despite apparent remission or recovery). More specifically, Stage 1 is the prodromal phase -that is the time interval between the onset of prodromal symptoms and the onset of the characteristic manifestations of the fully developed illness (Cosci & Fava, 2013). After the acute phase (Stage 2), it might be difficult to assess whether partial or full remission has occurred, and attenuated symptoms, the so-called residual symptoms, might be observed (Stage 3); they are due to partial persistence of the disorder or an aggravation of a pre-existing abnormal personality trait. Stage 4 represents chronicity of the psychiatric disorder (Cosci & Fava, 2013).

There appears to be a relationship between residual and prodromal symptoms. Detre and Jarecki (1971) provided a model defined as the rollback phenomenon: as the illness remits, it progressively recapitulates, albeit in reverse order. Certain prodromal symptoms may be overshadowed by the acute manifestations of the disorder, but they persist as residual symptoms and progress to become prodromes of relapse. Prodromal symptoms of relapse tend to mirror, in fact, those of the initial episode (Cosci & Fava, 2013). According to the rollback model, there is also a temporal relationship between the time of development of a disorder and the duration of the phase of recovery. This has several exemplifications in clinics. For instance, the persistence of residual symptoms after an antidepressant treatment administered to treat a major depressive episode represents a risk of relapse which should be considered by clinicians and considered as a partial response to the antidepressant treatment administered (Tomba & Fava, 2012).

Assessing Side Effects

Evidence Based Medicine is focused on the potential benefits that therapy may entail as to baseline risk, but it is likely to neglect, in addition to responsiveness, also vulnerabilities (Fava, 2017; Richardson & Doster, 2014). A rational approach to treatment considers the balance between potential benefits and adverse effects applied to the individual patient (Fava, 2017; Vandenbroucke & Psaty, 2008). The achievement of such balance is hindered by the difficult integration of different sources of information.

Several side effects of psychotropic medications are transient and may disappear after a few weeks following treatment initiation, but potentially serious adverse events may persist or ensue later. Antidepressants' side effects encompass gastrointestinal symptoms (e.g., nausea, diarrhea, gastric bleeding, dyspepsia), hepatotoxicity, weight gain and metabolic abnormalities, cardiovascular disturbances (e.g., heart rate, QT interval prolongation, hypertension, orthostatic hypotension), genitourinary symptoms (e.g., urinary retention, incontinence), sexual dysfunction, hyponatremia, osteoporosis and risk of fractures, bleeding, central nervous system disturbances (e.g., lowering of seizure threshold, extrapyramidal side effects, cognitive disturbances), sweating, sleep disturbances, affective disturbances (e.g., apathy, switches, paradoxical effects), ophthalmic manifestations (e.g., glaucoma, cataract) and hyperprolactinemia (Carvalho, Sharma, Brunoni, Vieta, & Fava, 2016).

Long-term use of antidepressants such as Serotonin Selective Reuptake Inhibitors (SSRI) may induce weight gain, after an initial period characterized by reduced appetite, and the increased weight does not necessarily recede upon the drug discontinuation (Carvalho et al., 2016). It has been suggested that an increase in exposure to antidepressants via a multitude of mechanisms may be a driving force for the obesity pandemic (Lee, Paz-Filho, Mastronardi, Licinio, & Wong, 2016). Similarly, the prevalence of sexual side effects can be as high as 50-70% among individuals taking SSRIs and such effects

may persist even after discontinuation (Carvalho et al., 2016), the so-called post-SSRI sexual dysfunction (Bala, Nguyen, & Hellstrom, 2018).

Negative effects may also occur as a result of psychotherapeutic treatment, whether due to technique, patient or therapist variables, or inappropriate use (Barlow, Gorman, Shear, & Woods, 2000; Linden, 2013; Scott & Young, 2016). The side effects of psychotherapy are difficult to recognize because of the number of variables involved, including the various stages of the psychotherapeutic process (Linden, 2013).

Targets of assessment have predominantly involved the desired effects of a medication while the evaluation of adverse events has been often neglected, although they can be measured via both interviews and self-rated instruments. Assessing the side effects that occur with any type of drug treatment requires a careful clinimetric collection of symptoms in addition to medical laboratory and investigational methods. The UKU side effect rating scale (Lingjærde, Ahlfors, Bech, Dencker, & Elgen, 1987) is an example of scale that considerably improved the detection of side effects, because of its comprehensive nature. For instance, sexual side effects are common and yet are some of the most under-reported adverse effects associated with the use of antidepressants, and a growing body of evidence indicates that such side effects should be monitored by use of specific instruments (Balon & Segraves, 2008; Carvalho et al., 2016). Further, Karch and Lasagna (1975) noted that the history of toxicology reminds us vividly of the lag that often occurs between the first introduction of a drug into humans and the recognition of certain adverse events from that drug. There is a need to update specific instruments for side effects with findings that may derive from case reports and clinical observations. For instance, the wide range of side effects that may ensue with long-term treatment with second generation antidepressants (Carvalho et al., 2016) would require specific methods of investigation.

Behavioral Toxicity

In 1968, DiMascio and Shader provided a conceptual framework for behavioral toxicity of psychotropic drugs and defined behavioral toxicity as the pharmacological actions of a drug that, within the dose range in which it has been found to possess clinical utility, may produce alterations in mood, perceptual, cognitive, and psychomotor functions, which limit the capacity of the individual or constitute a hazard to his well-being (DiMascio & Shader, 1968). In 1980, Perl and colleagues pointed out that psychotropic drugs can cause behavioral toxicity through the extension of their primary therapeutic action and/or the onset of secondary actions as well as withdrawal, dependence, and tolerance symptoms (Perl, Hall, & Gardner, 1980).

The concept of behavioral toxicity encompasses adverse events that may be limited to the period of drug administration and/or persist long after their discontinuation. Any type of psychotropic drug treatment, particularly after long-term use, may increase the risk of experiencing additional psychopathological problems that do not necessarily sub-

side with discontinuation of the drug or of modifying responsiveness to subsequent treatments (Fava, Cosci, Offidani, & Guidi, 2016). These latter phenomena can be subsumed under the rubric of iatrogenic comorbidity (Fava et al., 2016).

"Iatrogenic comorbidity" refers to unfavorable modifications in the course, characteristics, and responsiveness of an illness that may be related to treatments administered previously (Fava et al., 2016). Such vulnerabilities may occur during treatment administration and/or manifest themselves after its discontinuation. The changes can be persistent and not limited to a short phase, such as in the case of withdrawal reactions, and cannot subsume under the generic rubrics of adverse events or side effects.

Behavioral toxicity may ensue with any type of medical drug. Examples related to antidepressant drug use may be the onset of suicidality and aggression, switching from unipolar to bipolar course, withdrawal phenomena upon discontinuation, post-withdrawal persistent disorders (Carvalho et al., 2016; Fava et al., 2016). Such phenomena require adequate clinimetric indices for their detection, as the late recognition of withdrawal syndromes after antidepressant discontinuation teaches (Chouinard & Chouinard, 2015).

Behavioral toxicity may apply also to drugs directed to medical conditions (Shader, 1972; Tisdale & Miller, 2010; Whitlock, 1981), which may induce depression, anxiety, and other psychiatric symptoms.

Examples of behavioral toxicity that are concerned with the use of antidepressant drugs encompass switching into mania or hypomania during treatment, both in bipolar disorder (Tondo, Vázquez, & Baldessarini, 2010) and in allegedly unipolar patients (Joseph, Youngstrom, & Soares, 2009; Offidani, Fava, Tomba, & Baldessarini, 2013); withdrawal symptoms following reduction or discontinuation of antidepressant treatment, in the form of acute withdrawal symptomatology or persistent post-withdrawal disorders (Chouinard & Chouinard, 2015). Such manifestations of behavioral toxicity may be easily misinterpreted as a sign of impending relapse or the need to keep the antidepressant at the same dosage. Untreated symptoms may be mild and resolve spontaneously in one to three weeks; in other cases, they may persist for months or even years (Chouinard & Chouinard, 2015). Their prevalence is unknown at the moment, due to their very recent definition. The high prevalence of mental disorders in the general population may also be an effect of the presence of disorders that are a consequence of previous pharmacological treatments (Cosci, Guidi, Balon, & Fava, 2015). For instance, much of the refractoriness to treatment of anxious depression may be actually due to persistent post-withdrawal disorders that are secondary to the use of antidepressant drugs in anxiety disorders (Fava & Tomba, 2014).

All these phenomena may be explained based on the oppositional model of tolerance. Continued drug treatment may recruit processes that oppose the initial acute effect of a drug. When drug treatment ends, these processes may operate unopposed, at least for some time and increase vulnerability to relapse (Fava & Offidani, 2011).

Interaction of Medical Drugs With Behavioral Variables and Psychotherapy

Each therapeutic act may be a result of multiple ingredients that can be specific or non-specific: expectations, preferences, motivation, illness behavior and patient-doctor interactions are examples of variables that may affect treatment outcome (Fava, Guidi, Rafanelli, & Rickels, 2017; Rickels, 1968; Schedlowski, Enck, Rief, & Bingel, 2015). Such variables may be the object of study of clinical pharmacopsychology.

In 1969, Uhlenhuth, Lipman, and Covi examined the combinations of pharmacotherapy and psychotherapy in psychiatric disorders. They outlined four models of interaction: a) addition (i.e., the effects of two interactions combined equals the sum of their individual effects); b) potentiation (i.e., the effect of two interventions combined is greater than the sum of their individual effects); c) inhibition (i.e., the effect of two interventions combined is less that each individual effect); d) reciprocation (i.e., the effect of the two interventions combined equals the individual effect of the more potent intervention). Most of the studies are compatible with the additive and reciprocal concepts of interaction (Cuijpers et al., 2014; Forand, de Rubeis, & Amsterdam, 2013; Guidi et al., 2018; Uhlenhuth et al., 1969). There are, however, some high quality and well-designed individual studies suggesting that addition of a benzodiazepine or an antidepressant to cognitive behavioral treatment of anxiety disorders could be detrimental compared to placebo at follow-up (Barlow et al., 2000; Haug et al., 2003; Marks et al., 1993; Nordahl et al., 2016), thus indicating an inhibitory effect of the interaction. Again, clinical pharmacopsychology could be crucial for disclosing the nature of these relationships.

The Setting for Clinical Pharmacopsychology

We illustrate here a Clinical Pharmacopsychology Service as an example of an innovative application of clinical psychology in the medical setting.

A Clinical Pharmacopsychology Service

The Service has been operating since 2018 at the Department of Health Sciences, University of Florence (Florence, Italy). This outpatient clinic is addressed to patients who are looking for treatment programs allowing to rationalize, reduce, and discontinue psychotropic medications. The Service is run by an experienced clinical psychologist from the University of Florence who has a special interest and training in psychopharmacology, psychotherapy, and psychosomatic medicine. The outpatient facility is open one day a week with space for a maximum of eight patients and at least one hour dedicated to each patient.

The clinical psychologist works jointly with two psychologists (providing psychotherapy) and two consultants (one internist and one psychiatrist with a strong back-

ground in psychopharmacology). The clinical psychologist makes the initial assessment and monitors treatment choices. Team members work in close coordination, with repeated assessments and sequential combination of treatments (Fava, Park, & Dubovsky, 2008).

The main source of referral is the webpage[1] of the Service that was created to disseminate knowledge on the clinical phenomenon of withdrawal after discontinuation of antidepressants. Usually, the patients already looked for an aide in their environment (e.g., the psychiatrist or the general practitioner who prescribed the medication) without success before asking for an aide at the Service.

The first visit at the Service is conducted as follows, although the order of the schedule could be changed as required:

- complete history of psychiatric/psychological aspects according to the principles of macro-analysis (see below);
- formulation of the case, also on the basis of clinimetric tools (Fava, Tomba, & Sonino, 2012, Fava, Rafanelli, & Tomba, 2012), staging (Cosci & Fava, 2013), subtyping of diagnostic categories (see below);
- in addition to psychiatric diagnoses according to the DSM, the patient is evaluated via the Diagnostic clinical Interview for Drug Withdrawal 1 (DID-W1) (Cosci, Chouinard, Chouinard, & Fava, 2018) and the Discontinuation-Emergent Signs and Symptoms (DESS) (Rosenbaum, Fava, Hoog, Ascroft, & Krebs, 1998) (see below);
- the clinical psychologist goes over the patient's documents and previous workup;
- appraisal of the present situation, based on all findings (including answers to the DID-W1 and the DESS) and patient education;
- discussion of treatment choices and prescriptions.

The Diagnostic clinical Interview for Drug Withdrawal 1 (DID-W1) – New Symptoms of Selective Serotonin Reuptake Inhibitors (SSRI) or Serotonin Norepinephrine Reuptake Inhibitors (SNRI) is a semi-structured interview assessing withdrawal syndromes according to Chouinard's diagnostic criteria (Cosci et al., 2018). Such criteria identify three different withdrawal syndromes: new withdrawal symptoms, rebound syndrome, and persistent post-withdrawal disorder. The Discontinuation-Emergent Signs and Symptoms (DESS) is a self-administered checklist of signs and symptoms which might occur after the discontinuation of SSRI.

We will give an exemplification of this approach with the following case.

The Case of Miss X.

In order to illustrate, in practice, the activities at the Service of Pharmacopsychology, we present a clinical case.

1) https://www.smettereglipsicofarmaci.unifi.it/changelang-eng.html

Miss X. came to our attention after having been visited by several psychiatrists who suggested she should maintain paroxetine, which had been prescribed 10 years earlier for a panic disorder diagnosis. She received this suggestion each time she tried to reduce paroxetine and had the occurrence of anxiety, panic attacks, and depressed mood.

At first visit, the patient did not satisfy DSM diagnostic criteria for psychiatric disorders. She was strongly determined to reduce paroxetine for the following reasons: she gained about 10 kilograms of weight in 10 years, she had dampened sexual desire, she had mild hyperglycaemia and she did not want to live with paroxetine any longer.

The clinical psychologist performed the macro-analysis (Fava & Tomba, 2014; Tomba & Fava, 2012), which allows to establish a relationship between co-occurring syndromes and problems based on where treatment should begin in the first place and assuming that there are functional relationships among problematic areas and that the targets of treatment may vary during the course of disturbances. For Miss X., the problematic areas were: past attempts to reduce paroxetine which invariably produced the reappraisal of anxiety, panic attacks, depressed mood, and failure to discontinue paroxetine weight gain; hyperglycaemia and sexual dysfunction.

Thereafter, microanalysis, a detailed analysis of symptoms for functional assessment (Emmelkamp, Bouman, & Scholing, 1993), was performed. It requires consideration of the onset of complaints, their course, circumstances that aggravate or ameliorate symptoms, short-term and long-term impact of symptoms on quality of life, and work and social adjustment (Emmelkamp et al., 1993), and may include specific tests and rating scales (Bech, 1993) which must be integrated into the rest of the assessment and not viewed in isolation (Emmelkamp et al., 1993). In the framework of the micro-analysis, both DESS and DID-W1 were proposed to Miss X. The DESS did not provide additional information. The DID-W1 disclosed that the patient met the criteria for past rebound syndrome. Thus, the problematic areas in the macro-analysis were updated as follows: past attempts to reduce paroxetine which failed; lifetime rebound syndromes; weight gain; hyperglycaemia and sexual dysfunction.

On the basis of the macro- and the micro-analysis, the clinical psychologist asked for the consultation of the internist and the psychiatrist. It was decided to taper and discontinue paroxetine. The aim was to limit weight gain, help to normalize the hyperglycaemia (probably due to an excessive intake of carbohydrates) and verify whether paroxetine discontinuation improved sexual dysfunction. The clinician deferred to a second stage assessment the determination of whether paroxetine reduction triggers a withdrawal syndrome (Chouinard & Chouinard, 2015).

At a second visit, which occurred eight days later and seven days after the reduction of paroxetine from 40 mg to 35 mg daily, Miss X. presented also anxiety and mood swings. The clinical psychologist ran again the macro- and micro-analysis, administered again DID-W1 and DESS and updated the problematic areas as follows: past attempts to reduce paroxetine which failed; lifetime rebound syndromes; weight gain; hyperglycae-

mia; sexual dysfunction; current rebound syndrome characterized by anxiety and mood swings. Via the diagnosis of rebound syndrome the clinician was able to subtype and differentiate within the broader diagnostic entity of withdrawal syndrome. At re-assessment, the clinical reasoning was also used and let the clinical psychologist go through a series of "transfer stations" where potential connections between presenting symptoms and pathophysiological process are drawn (Feinstein, 1973). Based on the re-assessment as well as on the clinical reasoning, the clinical psychologist proposed Miss X. the psychotherapeutic management suggested by Fava and Belaise (2018).

Accomplishments and Shortcomings

In brief, the assessment provided to patients incorporates variables such as type and duration of psychotropic medication treatment, patterns of symptoms, stage of illness, comorbid conditions, timing of phenomena, responses to previous attempts to discontinue, and other clinical distinctions that demarcate major prognostic and therapeutic differences among patients who otherwise seem to be deceptively similar since they share the same diagnosis and the same drug treatment. Such variables are filtered by the clinical judgment (Fava & Tomba, 2014; Tomba & Fava, 2012) which provides the following assessment strategies: the use of diagnostic transfer stations instead of diagnostic endpoints using repeated assessments, subtyping versus integration of different diagnostic categories, staging, macro- and micro-analysis (Fava, Rafanelli, & Tomba, 2012). During the treatment path, patients are reassessed after the first line of treatment has been completed to reconfirm the diagnosis and refine the treatment plan.

This service fills gaps that are left with ordinary psychiatric care, and provides a comprehensive assessment which goes beyond the DSM and includes clinimetric tools.

Of course, difficulties might emerge from a comprehensive assessment of this kind. At least two main practical issues should be raised. The first is that it is not easy to have these kinds of services as part of the national health system which commonly imposes a time constraint of 15-20 minutes per visit. Second, there is an economic load for the national health system or for the patient due to the high level of engagement of clinicians. However, if we use a medium/long-term perspective, we may see that the cost is only apparently high since the patients in the majority of cases stop medications and maintain a symptoms-free condition without needing further visits in future years.

Finally, a potential shortcoming of the service is that it does not cooperate with a laboratory which monitors drug blood levels which could be related to psychological withdrawal or treatment responses.

Conclusions

Clinical pharmacopsychology offers a unifying framework for the understanding of clinical phenomena in medical and psychiatric settings (Fava, Tomba, & Bech, 2017). Its domains encompass the clinical benefits of psychotropic drugs, the characteristics that predict responsiveness to treatment, the vulnerabilities induced by treatment (i.e., side effects, behavioral toxicity, iatrogenic comorbidity), and the interactions between drug treatment and psychological variables. Its aim is to provide a comprehensive assessment of the clinical important changes that are concerned with wanted and expected treatment effects; treatment-induced unwanted side effects; and the patient's own personal experience of a change in terms of well-being and/or quality of life. It is now time to practice clinical pharmacopsychology, creating ad hoc services in Europe.

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References

Bala, A., Nguyen, H. M. T., & Hellstrom, W. J. G. (2018). Post-SSRI sexual dysfunction: A literature review. *Sexual Medicine Reviews, 6*(1), 29-34. https://doi.org/10.1016/j.sxmr.2017.07.002

Balon, R., & Segraves, R. T. (2008). Survey of treatment practices for sexual dysfunction(s) associated with antidepressants. *Journal of Sex & Marital Therapy, 34*(4), 353-365. https://doi.org/10.1080/00926230802096390

Barlow, D. H., Gorman, J. M., Shear, M. K., & Woods, S. W. (2000). Cognitive behavioral therapy, imipramine and their combination for panic disorder. *Journal of the American Medical Association, 283*(19), 2529-2536. https://doi.org/10.1001/jama.283.19.2529

Bech, P. (1990). Measuring psychological distress and well-being. *Psychotherapy and Psychosomatics, 54*(2-3), 77-89. https://doi.org/10.1159/000288382

Bech, P. (1993). *Rating scales for psychopathology, health status and quality of life.* Berlin, Germany: Springer.

Bech, P. (2005). Social functioning: Should it become an endpoint in trials of antidepressants? *CNS Drugs, 19*(4), 313-324. https://doi.org/10.2165/00023210-200519040-00004

Bech, P. (2016). Clinimetric dilemmas in outcome scales for mental disorders. *Psychotherapy and Psychosomatics, 85*(6), 323-326. https://doi.org/10.1159/000448810

Carvalho, A. F., Sharma, M. S., Brunoni, A. R., Vieta, E., & Fava, G. A. (2016). The safety, tolerability and risks associated with the use of newer generation antidepressant drugs. *Psychotherapy and Psychosomatics, 85*(5), 270-288. https://doi.org/10.1159/000447034

Chouinard, G., & Chouinard, V.-A. (2015). New classification of selective serotonin reuptake inhibitor withdrawal. *Psychotherapy and Psychosomatics, 84*(2), 63-71. https://doi.org/10.1159/000371865

Clancy, C., & Collins, F. S. (2010). Patient-Center Outcomes Research Institute: The intersection of science and health care. *Science Translational Medicine, 2*(37), Article 37cm18. https://doi.org/10.1126/scitranslmed.3001235

Cosci, F., Chouinard, G., Chouinard, V.-A., & Fava, G. A. (2018). The Diagnostic Clinical Interview for Drug Withdrawal 1 (DID-W1) – New symptoms of selective serotonin reuptake inhibitors (SSRI) or serotonin noradrenaline reuptake inhibitors (SNRI): Inter-rater reliability. *Rivista di Psichiatria, 53*, 95-99. https://doi.org/10.1708/2891.29158

Cosci, F., & Fava, G. A. (2013). Staging of mental disorders: Systematic review. *Psychotherapy and Psychosomatics, 82*(1), 20-34. https://doi.org/10.1159/000342243

Cosci, F., Guidi, J., Balon, R., & Fava, G. A. (2015). Clinical methodology matters in epidemiology: Not all benzodiazepines are the same. *Psychotherapy and Psychosomatics, 84*(5), 262-264. https://doi.org/10.1159/000437201

Cuijpers, P., Sijbrandij, M., Koole, S. L., Andersson, G., Beekman, A. T., & Reynolds, C. F., III. (2014). Adding psychotherapy to antidepressant medication in depression and anxiety disorders: A meta-analysis. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA), 13*(1), 56-67. https://doi.org/10.1002/wps.20089

de Leon, J., Baca-Garcia, E., & Blasco-Fontecilla, H. (2015). From the serotonin model of suicide to a mental pain model of suicide. *Psychotherapy and Psychosomatics, 84*(6), 323-329. https://doi.org/10.1159/000438510

Derogatis, L. R., Lipman, R. S., Rickels, K., Uhlenmuth, E. H., & Covi, L. (1974). The Hopkins Symptom Checklist (HSCL): A measure of primary symptom dimensions. In P. Pichot (Ed.), *Psychological measurements in psychopharmacology* (pp. 79–110). Basel, Switzerland: Karger.

Detre, T. P., & Jarecki, H. (1971). *Modern psychiatric treatment.* Philadelphia, PA, USA: Lippincott.

DiMascio, A., & Shader, R. I. (1968). Behavioral toxicity of psychotropic drugs. *Connecticut Medicine, 32*, 617-620.

Emmelkamp, P. M. G., Bouman, T., & Scholing, A. (1993). *Anxiety disorders.* Chichester, United Kingdom: Wiley.

Eysenck, H. J. (1963). *Experiments with drugs.* Oxford, United Kingdom: Pergamon Press.

Fava, G. A. (1996). The concept of recovery in affective disorders. *Psychotherapy and Psychosomatics, 65*(1), 2-13. https://doi.org/10.1159/000289025

Fava, G. A. (2017). Evidence-based medicine was bound to fail: A report to Alvan Feinstein. *Journal of Clinical Epidemiology, 84*, 3-7. https://doi.org/10.1016/j.jclinepi.2017.01.012

Fava, G. A., & Bech, P. (2016). The concept of euthymia. *Psychotherapy and Psychosomatics, 85*(1), 1-5. https://doi.org/10.1159/000441244

Fava, G. A., & Belaise, C. (2018). Discontinuing antidepressant drugs: Lesson from a failed trial and extensive clinical experience. *Psychotherapy and Psychosomatics, 87*(5), 257-267. https://doi.org/10.1159/000492693

Fava, G. A., Cosci, F., Offidani, E., & Guidi, J. (2016). Behavioral toxicity revisited: Iatrogenic comorbidity in psychiatric evaluation and treatment. *Journal of Clinical Psychopharmacology, 36*(6), 550-553. https://doi.org/10.1097/JCP.0000000000000570

Fava, G. A., Cosci, F., & Sonino, N. (2017). Current psychosomatic practice. *Psychotherapy and Psychosomatics, 86*(1), 13-30. https://doi.org/10.1159/000448856

Fava, G. A., Guidi, J., Rafanelli, C., & Rickels, K. (2017). The clinical inadequacy of the placebo model and the development of an alternative conceptual framework. *Psychotherapy and Psychosomatics, 86*(6), 332-340. https://doi.org/10.1159/000480038

Fava, G. A., & Offidani, E. (2011). The mechanisms of tolerance in antidepressant action. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 35*(7), 1593-1602. https://doi.org/10.1016/j.pnpbp.2010.07.026

Fava, G. A., Park, S. K., & Dubovsky, S. L. (2008). The mental health clinic: A new model. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA), 7*(3), 177-181. https://doi.org/10.1002/j.2051-5545.2008.tb00192.x

Fava, G. A., Rafanelli, C., & Tomba, E. (2012). The clinical process in psychiatry: A clinimetric approach. *The Journal of Clinical Psychiatry, 73*(2), 177-184. https://doi.org/10.4088/JCP.10r06444

Fava, G. A., & Tomba, E. (2014). Treatment of comorbid anxiety disorders and depression. In P. M. G. Emmelkamp & T. Ehring (Eds.), *The Wiley handbook of anxiety disorders* (pp. 1165-1182). New York, NY, USA: John Wiley & Sons.

Fava, G. A., Tomba, E., & Bech, P. (2017). Clinical pharmapsychology: Conceptual foundations and emerging tasks. *Psychotherapy and Psychosomatics, 86*(3), 134-140. https://doi.org/10.1159/000458458

Fava, G. A., Tomba, E., & Sonino, N. (2012). Clinimetrics: The science of clinical measurements. *International Journal of Clinical Practice, 66*(1), 11-15. https://doi.org/10.1111/j.1742-1241.2011.02825.x

Feinstein, A. R. (1973). An analysis of diagnostic reasoning: I. The domains and disorders of clinical macrobiology. *The Yale Journal of Biology and Medicine, 46*, 212-232.

Feinstein, A. R. (1987). *Clinimetrics.* New Haven, CT, USA: Yale University Press.

Forand, N. R., de Rubeis, R. J., & Amsterdam, J. D. (2013). Combining medication and psychotherapy in the treatment of major mental disorders. In M. J. Lambert (Ed.), *Bergin and Garfield's handbook of psychotherapy and behavior change* (6th ed. pp. 735-774). Hoboken, NJ, USA: Wiley.

Guidi, J., Brakemeier, E. L., Bockting, C. L. H., Cosci, F., Cuijpers, P., Jarrett, R. B., . . . Fava, G. A. (2018). Methodological recommendations for trials of psychological interventions. *Psychotherapy and Psychosomatics, 87*(5), 276-284. https://doi.org/10.1159/000490574

Guidi, J., Fava, G. A., Bech, P., & Paykel, E. (2011). The clinical interview for depression. *Psychotherapy and Psychosomatics, 80*(1), 10-27. https://doi.org/10.1159/000317532

Hamilton, M. (1974). General problems of psychiatric rating scales (especially for depression). In P. Pichot (Ed.), *Psychological measurements in psychopharmacology* (pp. 125-138). Basel, Switzerland: Karger.

Haug, T. T., Blomhoff, S., Hellstrom, K., Holme, I., Humble, M., Madsbu, H. P., & Wold, J. E. (2003). Exposure therapy and sertraline in social phobia: 1-year follow-up of a randomised controlled trial. *The British Journal of Psychiatry, 182*(4), 312-318. https://doi.org/10.1192/bjp.182.4.312

Horwitz, R. I., Hayes-Conroy, A., & Singer, B. H. (2017). Biology, social environment, and personalized medicine. *Psychotherapy and Psychosomatics, 86*(1), 5-10. https://doi.org/10.1159/000452134

Horwitz, R. I., Singer, B. H., Makuch, R. W., & Viscoli, C. M. (1996). Can treatment that is helpful on average be harmful to some patients? A study of the conflicting information needs of clinical inquiry and drug regulation. *Journal of Clinical Epidemiology, 49*(4), 395-400. https://doi.org/10.1016/0895-4356(95)00058-5

Janke, W. (1983) Response variability to psychotropic drugs: Overview of the main approaches to differential pharmacopsychology. In W. Janke (Ed.), *Response variability to psychotropic drugs* (pp. 33-65). Oxford, United Kingdom: Pergamon Press.

Janke, W., Debus, G., & Erdmann, G. (2000). Pharmacopsychology in Germany. In T. A. Ban, D. Healy, & E. Shorter (Eds.), *The triumph of psychopharmacology and the history of CINP* (pp. 152-157). Budapest, Hungary: Animula.

Janke, W., & Netter, P. (2004) Differentielle Pharmakopsychologie. In K. Pawlik (Ed.), *Enzyklopädie der Psychologie, Serie VIII: Differentielle Psychologie und Persönlichkeitsforschung, Band 5: Theorien und Anwendungsfelder der Differentiellen Psychologie* (pp. 925–1020). Göttingen, Germany: Hogrefe.

Joseph, M. F., Youngstrom, E. A., & Soares, J. C. (2009). Antidepressant-coincident mania in children and adolescents treated with selective serotonin reuptake inhibitors. *Future Neurology, 4*(1), 87-102. https://doi.org/10.2217/14796708.4.1.87

Karch, F. E., & Lasagna, L. (1975). Adverse drug reactions: A critical review. *Journal of the American Medical Association, 234*(12), 1236-1241. https://doi.org/10.1001/jama.1975.03260250028021

Kraepelin, E. (1892). *Ueber die Beeinflussung einfacher psychischer Vorgänge durch einige Arzneimittel.* Jena, Germany: Fischer.

Lee, S. H., Paz-Filho, G., Mastronardi, C., Licinio, J., & Wong, M. L. (2016). Is increased antidepressant exposure a contributory factor to the obesity pandemic? *Translational Psychiatry, 6*(3), Article e759. https://doi.org/10.1038/tp.2016.25

Linden, M. (2013). How to define, find and classify side effects in psychotherapy: From unwanted events to adverse treatment reactions. *Clinical Psychology & Psychotherapy, 20*(4), 286-296. https://doi.org/10.1002/cpp.1765

Lingjærde, O., Ahlfors, U. G., Bech, P., Dencker, S. J., & Elgen, K. (1987). The UKU side effect rating scale: A new comprehensive rating scale for psychotropic drugs and a cross-sectional study of side effects in neuroleptic-treated patients. *Acta Psychiatrica Scandinavica, 76*(s334), 1-100. https://doi.org/10.1111/j.1600-0447.1987.tb10566.x

Lipton, M. A. L., Di Mascio, A., & Killam, K. F. (1977). *Psychopharmacology: A generation of progress.* New York, NY, USA: Raven Press.

Marks, I. M., Swinson, R. P., Basoglu, M., Kuch, K., Noshirvani, H., O'Sullivan, G., . . . Wickwire, K. (1993). Alprazolam and exposure alone and combined in panic disorder with agoraphobia. *The British Journal of Psychiatry, 162*(6), 776-787. https://doi.org/10.1192/bjp.162.6.776

Nordahl, H. M., Vogel, P. A., Morken, G., Stiles, T. C., Sandvik, P., & Wells, A. (2016). Paroxetine, cognitive therapy or their combination in the treatment of social anxiety disorder with or without avoidant personality disorder. *Psychotherapy and Psychosomatics, 85*(6), 346-356. https://doi.org/10.1159/000447013

Offidani, E., Fava, G. A., Tomba, E., & Baldessarini, R. J. (2013). Excessive mood elevation and behavioral activation with antidepressant treatment of juvenile depressive and anxiety disorders. *Psychotherapy and Psychosomatics, 82*(3), 132-141. https://doi.org/10.1159/000345316

Perl, M., Hall, R. C. W., & Gardner, E. R. (1980). Behavioral toxicity of psychiatric drugs. In R. C. W. Hall (Ed.), *Psychiatric presentations of medical illness* (pp. 311-336). New York, NY, USA: Spectrum Publications.

Pichot, P. (1974). Introduction. In P. Pichot (Ed.), *Psychological measurements in psychopharmacology* (pp. 1-7). Basel, Switzerland: Karger.

Richardson, W. S., & Doster, L. M. (2014). Comorbidity and multimorbidity need to be placed in the context of a framework of risk, responsiveness, and vulnerability. *Journal of Clinical Epidemiology, 67*(3), 244-246. https://doi.org/10.1016/j.jclinepi.2013.10.020

Rickels, K. (1968). *Non-specific factors in drug therapy.* Springfield, IL, USA: Charles C. Thomas.

Rosenbaum, J. F., Fava, M., Hoog, S. L., Ascroft, C., & Krebs, W. B. (1998). Selective serotonin reuptake inhibitor discontinuation syndrome: A randomized clinical trial. *Biological Psychiatry, 44*(2), 77-87. https://doi.org/10.1016/S0006-3223(98)00126-7

Rothschild, A. J., Raskin, J., Wang, C. N., Marangell, L. B., & Fava, M. (2014). The relationship between change in apathy and changes in cognition and functional outcomes in currently non-depressed SSRI-treated patients with major depressive disorder. *Comprehensive Psychiatry, 55*(1), 1-10. https://doi.org/10.1016/j.comppsych.2013.08.008

Schedlowski, M., Enck, P., Rief, W., & Bingel, U. (2015). Neuro-bio-behavioral mechanisms of placebo and nocebo responses: Implications for clinical trials and clinical practice. *Pharmacological Reviews, 67*(3), 697-730. https://doi.org/10.1124/pr.114.009423

Scott, J., & Young, A. H. (2016). Psychotherapies should be assessed for both benefit and harm. *The British Journal of Psychiatry, 208*(3), 208-209. https://doi.org/10.1192/bjp.bp.115.169060

Shader, R. I. (1972). *Psychiatric complications of medical drugs.* New York, NY, USA: Raven Press.

Tisdale, J. E., & Miller, D. A. (2010). *Drug-induced diseases* (2nd ed.). Bethesda, MD, USA: American Society of Health-System Pharmacists.

Tomba, E., & Fava, G. A. (2012). Treatment selection in depression: The role of clinical judgment. *The Psychiatric Clinics of North America, 35*(1), 87-98. https://doi.org/10.1016/j.psc.2011.11.003

Tondo, L., Vázquez, G., & Baldessarini, R. J. (2010). Mania associated with antidepressant treatment: Comprehensive meta-analytic review. *Acta Psychiatrica Scandinavica, 121*(6), 404-414. https://doi.org/10.1111/j.1600-0447.2009.01514.x

Topp, C. W., Østergaard, S. D., Søndergaard, S., & Bech, P. (2015). The WHO-5 Well-Being Index: A systematic review of the literature. *Psychotherapy and Psychosomatics, 84*(3), 167-176. https://doi.org/10.1159/000376585

Tyrer, P., Tyrer, H., & Guo, B. (2016). The general neurotic syndrome: A re-evaluation. *Psychotherapy and Psychosomatics, 85*(4), 193-197. https://doi.org/10.1159/000444196

Uhlenhuth, E. H., Lipman, R. S., & Covi, L. (1969). Combined pharmacotherapy and psychotherapy. *The Journal of Nervous and Mental Disease, 148*(1), 52-64. https://doi.org/10.1097/00005053-196901000-00006

Vandenbroucke, J. P., & Psaty, B. M. (2008). Benefits and risks of drug treatments: How to combine the best evidence on benefits with the best data about adverse effects. *Journal of the American Medical Association, 300*, 2417-2419. https://doi.org/10.1001/jama.2008.723

Verrocchio, M. C., Carrozzino, D., Marchetti, L., Andreasson, K., Fulcheri, M., & Bech, P. (2016). Mental pain and suicide: A systematic review of the literature. *Frontiers in Psychiatry, 7*, Article 108. https://doi.org/10.3389/fpsyt.2016.00108

Whitlock, F. A. (1981). Adverse psychiatric reactions to modern medication. *The Australian and New Zealand Journal of Psychiatry, 15*(2), 87-103. https://doi.org/10.3109/00048678109159417

Clinical Psychology in Europe

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Scientific Update and Overview

Psychoneuroendocrinology and Clinical Psychology

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Abstract

Background: Hormones impact on cognition, emotions, and behaviour. Given that mental disorders are defined by abnormalities in these very same domains, clinical psychologists may benefit from learning more about alterations in endocrine systems, how they can contribute to symptoms commonly experienced by patients, and how such knowledge may be put to use in clinical practice.

Method: The aim of the present scientific update was to provide a brief overview of endocrine research relevant to the aetiology, diagnostics, and treatment of mental disorders, including some of the latest studies in this area.

Results: Hormones appear to be intrinsic to the development and maintenance of mental disorders. Oxytocin is involved in social cognition and behaviour and as such may be relevant to mental disorders characterised by social deficits (e.g., autism spectrum disorder and schizophrenia). Stress and sex steroids exert demonstrable effects on mood and cognition. In patients with depression and anxiety disorders, initial attempts to lower/enhance such hormones have thus been undertaken within conventional therapies in order to improve outcomes. Finally, hunger and satiety hormones may be involved in the vicious circle of dysfunctional eating behaviours and weight loss/gain in anorexia or bulimia nervosa.

Conclusion: Three conclusions can be drawn from this review: First, endocrine research should be considered when patients and clinicians are developing multidimensional illness models together. Second, endocrine markers can complement conventional assessments to provide a more comprehensive account of a patient's current state. Third, endocrine testing may guide treatment choices and inform the development of novel treatments.

Keywords

anxiety, cognition, depression, hormones, mental disorders, mood, psychological therapy

Highlights

- Hormones are intrinsic to the development and maintenance of mental disorders
- Endocrine research should be incorporated into multidimensional illness models
- Endocrine markers can complement conventional diagnostic assessments
- Endocrine testing may guide treatment choices and inform the development of new treatments

Psychoneuroendocrinology is an interdisciplinary research area dedicated to the interaction between the mind, brain, and hormonal system (Wolf & Saucier, 2013). Stress and lifestyle behaviours (e.g., diet, physical activity) are the most frequently studied *psychological* factors exerting short- and long-term effects on hormones. Conversely, a number of *hormones* are known to impact on psychological domains, such as cognition, emotions, and behaviour. Among these are hormones involved in social interaction (e.g., oxytocin), stress hormones (e.g., noradrenaline and cortisol), sex hormones (e.g., testosterone, oestradiol, and progesterone), and hormones involved in hunger and satiety (e.g., ghrelin, leptin, or insulin). Given that mental disorders are characterised by abnormalities in cognition, emotions, and behaviour, clinical psychologists may benefit from learning more about alterations in endocrine systems, how they may contribute to symptoms commonly experienced by patients, and how such knowledge may be put to use in clinical practice.

The aim of the present scientific update was therefore to provide a brief overview of endocrine research relevant to the aetiology, diagnostics, and psychopharmacological and psychotherapeutic treatment of mental disorders, including some of the latest studies in this area. Findings will be presented separately for each of the aforementioned domains and summarised in the final part of the manuscript alongside recommendations for clinical applications.

How Hormones Affect Social Interaction

The most prominent hormone regulating social interaction is oxytocin (Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011). Although oxytocin is available in the periphery (e.g., in reproductive organs), its central origin is in the hypothalamus, and oxytocin receptors are widely expressed in numerous areas of the brain, including the frontal cortex, amygdala, and olfactory nucleus.

Oxytocin has demonstrable effects on social cognition and behaviour, such as enhancing theory of mind, emotional recognition, empathy, social exploration, and attachment

(see also Ditzen et al., 2009; Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). As such, it has attracted the interest of researchers studying mental disorders characterised by social deficits, including autism spectrum disorders and schizophrenia. There is now evidence to suggest that oxytocin may be an aetiological factor in autism spectrum disorder, since several polymorphisms within the gene encoding its receptor (*OXTR*) have been found to be risk-inducing (Kranz et al., 2016; LoParo & Waldman, 2015). On the other hand, peripheral levels of oxytocin are often found to be unaltered in the same patients as well as in patients with psychotic disorders (Rutigliano et al., 2016). These null-findings need to be interpreted with caution, however, since the bioavailability of oxytocin in blood, urine, or saliva does not necessarily reflect its centrally circulating levels (Valstad et al., 2017), which are of greater importance considering the clinical features of these illnesses. Importantly, central levels are only quantifiable in humans via access to the cerebrospinal fluid by means of lumbar puncture. Thus, although it is unlikely that oxytocin levels will be used as a diagnostic illness marker in the near future, their potential role in the pathophysiology of disorders characterised by social deficits can be incorporated into psychoeducation delivered to patients and their next of kin.

Another line of research has examined the effects of intranasally administered oxytocin in patients with autism spectrum disorder and schizophrenia (Keech, Crowe, & Hocking, 2018), with findings of small but significant improvements in theory of mind (but not in emotion recognition or empathy). In other words, patients receiving exogenous oxytocin showed an increased ability to attribute mental states to others, thus providing ex juvantibus evidence for an involvement of the oxytocin system in the pathophysiology of these disorders. Importantly, numerous open questions need to be answered before oxytocin can be considered as an adjunct treatment for autism spectrum disorder or schizophrenia, including its precise mechanisms of action in the brain, its long-term efficacy, and potential adverse effects (e.g., increased irritability).

Interestingly, more recent research has explored the role of *endogenous* oxytocin as a modulator of treatment outcomes. A pilot study was able to demonstrate that the lower depressed patients' pre-treatment oxytocin levels, the lower their degree of change in a self-report measure of depression over the course of psychological therapy (Jobst et al., 2018). This finding aligns well with another study in patients with depressive disorders, which showed that oxytocin levels fluctuated during therapy sessions, and in parallel with subtle changes in the therapeutic alliance (i.e., ruptures; Zilcha-Mano, Porat, Dolev, & Shamay-Tsoory, 2018). Together, these studies suggest that oxytocin levels may also be a useful prognostic tool as well as a means to monitor treatment progress.

How Hormones Affect Cognition, Mood, and Sexual Function

Up to now, the largest share of clinical neuroendocrine research has been dedicated to the stress hormones noradrenaline and cortisol. The catecholamine noradrenaline (NA) is available in the brain and in several other body tissues (Fischer & Nater, 2015). Its central origin is the locus coeruleus, with α- and β-adrenergic receptors expressed in numerous other brain areas, such as the cortex, thalamus, hippocampus, amygdala, and hypothalamus. In the periphery, NA, together with adrenaline, is the main end product of the sympathetic nervous system, and its receptors are present in all major organs and cells of the immune system.

Noradrenaline has effects on multiple domains of psychological functioning, including cognition, affect, arousal, and pain perception. It is thus unsurprising that 1) cognitive symptoms (e.g., deficits in working memory), as experienced, for instance, by patients with depressive disorders (Maletic, Eramo, Gwin, Offord, & Duffy, 2017), 2) anxiety and hyperarousal, representing key clinical features of panic disorder and post-traumatic stress disorder (Bandelow et al., 2017), and 3) bodily symptoms such as fatigue and pain, which feature prominently in somatic symptom disorders (Nater, Fischer, & Ehlert, 2011), are all paralleled by altered NA functioning. Notably, findings are highly complex; depending on the tissue (i.e., different areas within the brain, blood), both elevated and attenuated concentrations of NA are observed, sometimes within the same patient cohort.

Drugs targeting the NA system (e.g., venlafaxine) constitute effective antidepressants and anxiolytics (e.g., Bandelow et al., 2014; DGPPN et al., 2015), thus adding further evidence to the assumption that the NA system is instrumental in the pathophysiology of depressive and anxiety disorders. Clinicians administering such drugs are advised to explain the role of NA to patients before initiating treatment. By contrast, in somatic symptom disorders and in physical diseases, it is mainly the peripheral actions of NA (e.g., its effects on the musculoskeletal or cardiovascular system) which are critical. Interestingly, in patients undergoing coronary artery bypass graft surgery, it was recently shown that preoperative psychological interventions led to significantly lower (i.e., more adaptive) levels of adrenaline after surgery when compared to standard medical care (Salzmann et al., 2017). This finding highlights the value of catecholamines as markers of therapeutic efficacy. Notably, NA activity can also be determined non-invasively, namely via salivary alpha-amylase, an enzyme involved in the digestion of starch, thus facilitating its use in clinical practice (Nater & Rohleder, 2009).

The glucocorticoid cortisol, the other major stress hormone, is the end point of the hypothalamic-pituitary-adrenal (HPA) axis (Ehlert, 2011). Although cortisol is synthesised in the adrenal cortex, both central (e.g., the hippocampus) and peripheral tissues (e.g., lymphocytes) are densely populated by mineralocorticoid and glucocorticoid recep-

tors. Apart from the gluconeogenetic and anti-inflammatory effects of cortisol, one of its main effects lies in influencing cognition.

Akin to the findings on NA, cortisol concentrations have been found to be abnormal in a number of patients presenting with cognitive problems (e.g., difficulty concentrating), as is the case in affective disorders (Belvederi Murri et al., 2016; Stetler & Miller, 2011). Moreover, abnormal cortisol concentrations have been demonstrated in patients with post-traumatic stress disorder, where they may contribute to re-experiencing of trauma via constant retrieval of the fear memory (Morris, Compas, & Garber, 2012), and in somatic symptom disorders, where they may contribute to bodily complaints (Tak et al., 2011). Interestingly, while patients with affective disorders are characterised by comparably elevated levels of cortisol (i.e., *hyper*cortisolism), patients with posttraumatic stress disorder or somatic symptom disorders mostly exhibit diminished levels (i.e., *hypo*cortisolism; Ehlert, Gaab, & Heinrichs, 2001; Heim, Ehlert, & Hellhammer, 2000). These differences may be attributable to different genetic predispositions and/or different amounts of stress experienced during the lifespan (Ehlert, 2013). Together, these findings underline the potential of cortisol for improving differential diagnostics.

These findings have been extended by clinical studies, where a similar dichotomy appears to prevail. In *depression*, the current state of research suggests that the higher a patient's pre-treatment cortisol levels, the lower their chances of responding to psychological therapy (Fischer, Strawbridge, Herane Vives, & Cleare, 2017). In addition, initial attempts to improve memory performance in these patients have been undertaken using agents which act on glucocorticoid receptors (e.g., mifepristone) or influence cortisol synthesis (e.g., ketoconazole; Soria et al., 2018). In *anxiety disorders*, the pattern seems to be reversed, insofar as lower cortisol levels predict worse treatment outcomes (Fischer & Cleare, 2017), although importantly, this only appears to be true for stimulated cortisol as measured during exposure sessions. This has been interpreted as an implication that a certain amount of cortisol is a prerequisite for patients to form an extinction memory, which is one of the key mechanisms underlying successful treatment for fear-related illnesses. More recent research suggests that this knowledge may be utilised to optimise exposure-based psychological therapy for anxiety disorders. For instance, Meuret et al. (2016) were able to demonstrate that early-day exposure sessions (i.e., when endogenous cortisol levels are highest) led to greater clinical improvement in patients with panic disorder and agoraphobia when compared to sessions held later on during the day.

Sex hormones, such as testosterone, oestradiol, and progesterone, are end products of the hypothalamic-pituitary-gonadal (HPG) axis (Melcangi, Giatti, & Garcia-Segura, 2016). They are mainly produced in the testes in men and in the ovaries in women, and their key function is to orchestrate reproduction and sexual functioning. However, sex steroids also act as neurosteroids (e.g., fostering neurogenesis and differentiation) in various parts of the brain, such as the hippocampus and prefrontal cortex.

In terms of mental disorders, the bulk of research to date has studied the role of sex steroids in sexual dysfunctions. Testosterone, for instance, is lowered in men with erectile disorder (Isidori et al., 2014), and hormonal (replacement) therapy has been proven to be useful in enhancing erectile function in hypogonadal men (Corona et al., 2017; Elliott et al., 2017) and sexual function in post-menopausal women (Elraiyah et al., 2014). However, long-term follow-up studies are scarce and potential adverse effects of exogenous testosterone (e.g., acne) need to be carefully weighed against the benefits. Similarly, oestrogens and combined oestrogen/progestogen treatments appear to enhance sexual function in some post-menopausal women (Nastri et al., 2013), but again, side effects need to be considered. These findings are important for any clinical psychologist advising patients with sexual dysfunctions in terms of adjunct treatments.

A burgeoning literature also demonstrates the involvement of sex hormones in other mental disorders, which is attributable to the aforementioned central expression of steroid receptors. In schizophrenia, it was shown that oestradiol and selective oestradiol receptor modulators (e.g., raloxifene) can enhance memory and executive functions (Soria et al., 2018). In addition, recent research suggests that sex steroids may exert positive effects on mood. For instance, longer lifetime exposure to endogenous and exogenous oestradiol was found to be linked to fewer depressive symptoms during the menopausal transition (Marsh et al., 2017), whereas greater fluctuations in endogenous oestradiol during the menopausal transition predicted more depressive symptoms in women reporting high amounts of stress (Gordon, Rubinow, Eisenlohr-Moul, Leserman, & Girdler, 2016). These findings not only contribute to a more profound understanding of the symptoms pertaining to psychotic and mood disorders, but may ultimately be put to use in order to guide (sex-oriented) treatment choices.

How Hormones Affect Hunger and Satiety

A number of hormones regulating hunger and satiety, such as ghrelin, leptin, or insulin, have been related to different mental disorders (Drobnjak & Ehlert, 2011). Whereas the orexigenic hormone ghrelin is produced in the stomach, the anorexic hormones leptin and insulin are produced in adipose tissue and in the pancreas, respectively. All three hormones are capable of crossing the blood-brain barrier and thus directly influence energy homoeostasis by acting on the hypothalamus.

Ghrelin, leptin, and insulin have, for the most part, been objects of research into eating disorders. For instance, enhanced baseline ghrelin levels were reported in patients with eating disorders (Prince, Brooks, Stahl, & Treasure, 2009), likely as a consequence of restrained eating. Importantly, elevated levels of ghrelin may in turn facilitate other dysfunctional behaviours, such as hoarding food in anorexia nervosa or binge eating in bulimia nervosa or binge eating disorder. Furthermore, patients with anorexia nervosa have been found to present with *increased* insulin sensitivity, whereas patients with bulimia

nervosa or binge eating disorder exhibit *decreased* insulin sensitivity (Ilyas et al., 2018). Similar to ghrelin, these findings have been interpreted as being the result of dietary restriction and weight loss/weight gain, respectively, while at the same time further contributing to dysfunctional eating patterns by affecting appetite regulation in the brain (i.e., diminishing/enhancing appetite). This is important knowledge when trying to make sense of the vicious circles that perpetuate eating disorders.

Evidence is now also accumulating that hunger and satiety hormones are abnormal in other mental disorders, mainly those presenting with metabolic symptoms and/or comorbid metabolic diseases (e.g., diabetes mellitus). Findings include elevated levels of leptin and insulin resistance in patients with psychotic disorders (Greenhalgh et al., 2017; Pillinger et al., 2017; Stubbs, Wang, Vancampfort, & Miller, 2016) and depressive disorders (Kan et al., 2013). Notably, these seem to be independent of BMI and intake of antipsychotic medication (which are known to have several metabolic side effects). This suggests that these hormonal abnormalities are not a mere consequence of lifestyle behaviours associated with suffering from a chronic illness, but may be antecedents of highly debilitating ancillary symptoms pertaining to psychotic and depressive disorders.

Importantly, recent studies support the notion that endogenous ghrelin and leptin may also influence treatment outcomes: Whereas increases in ghrelin predicted non-responses to treatment with lithium-augmented antidepressants in patients with depression (Ricken et al., 2017), leptin was positively linked to increases in BMI (Ricken et al., 2016). In terms of ghrelin, the observed increases in non-responders could be interpreted as being secondary to reduced appetite, a core symptom of severe depression. In terms of leptin, synergistic actions with lithium on the serotonergic system could have resulted in an attenuation of leptin's anorexic effect, but more research is warranted to investigate the intricate interplay between the two systems. These findings are important to consider by clinicians prescribing psychoactive drugs, and will hopefully allow the adjusting of treatments to the needs of the individual patient in the future.

Summary and Integration

It is evident from this brief overview that hormones are intrinsic to both the development and maintenance of mental disorders, and there are several conceivable ways in which this knowledge may be useful to clinical psychology. First, neuroendocrine research should find its way into clinical practice when clinicians and patients are developing multidimensional illness models together, such as at the beginning of psychological therapy. This is important given that mental disorders are still stigmatised by a large proportion of the general population due to lay concepts about their origins (e.g., depressive disorders being seen as a lack of willpower). Second, endocrine markers may be used to aid the (differential) diagnostics of mental disorders. This is important in light of the fact that not all aspects of mental health are accessible by means of introspection, let alone by in-

dividuals who suffer from deficits in detecting and reporting signs of psychological distress (e.g., those scoring high on alexithymia). Similarly, hormones may be used to assess treatment outcomes above and beyond self-report symptom measures or clinical rating scales. These ideas align well with the US National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC), which aim to provide more precise characterisations of a patient by integrating biological and psychological research (e.g., Insel et al., 2010). To this end, a matrix combining five psychological domains (social processes, arousal/regulation, negative valence, positive valence, and cognition) with different units of analysis (genes, molecules, cells, neural circuits, physiology, behaviour, self-reported information, and paradigms) has been proposed. This allows for a particular state of mental illness to be described by deficits in different psychological domains, which map on to specific biological substrates (e.g., neuroendocrine abnormalities). Third, the results of neuroendocrine testing may guide treatment choices, that is, they may support clinicians in finding out what is likely to work for whom and why. This resonates well with the central tenet of precision psychiatry, which advocates the tailoring of treatments to the needs of the individual patient by integrating data from multiple levels of information (e.g., biological, personality, and behavioural measures). On a related note, alternative or additional treatments for mental disorders may be developed that are based on a more in-depth account of patients' pathophysiology (e.g., hormonal substitution as an augmentation to psychological therapy).

In the foreseeable future, clinical psychology is likely to benefit from a number of emerging trends in psychoneuroendocrinological research. Elucidating the genetic and epigenetic underpinnings of endocrine functioning will be crucial to fully comprehend its role in mental disorders. As both the distribution and sensitivity of endocrine receptors are governed by genetic variation as well as by the individual's epigenetic make-up (e.g., DNA methylation), this could ultimately enable the identification of patients who run the risk of developing mental illnesses. Similarly, learning more about the cross-talk between different endocrine systems and between endocrine and other bodily systems (e.g., central monoaminergic systems) should allow for a more accurate description of how, precisely, endocrine disturbances contribute to the onset of mental disorders – and provide more precise targets for additional or alternative treatment options. Finally, the advent of novel methodologies to assess hormones in a reliable, non-invasive manner (e.g., fingernail cortisol) holds the promise to translate neuroendocrine knowledge into clinical practice – and hopefully to the benefit of patients and clinical psychologists alike.

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References

Bandelow, B., Baldwin, D., Abelli, M., Bolea-Alamanac, B., Bourin, M., Chamberlain, S. R., . . . Riederer, P. (2017). Biological markers for anxiety disorders, OCD and PTSD: A consensus statement. Part II: Neurochemistry, neurophysiology and neurocognition. *The World Journal of Biological Psychiatry, 18*(3), 162-214. https://doi.org/10.1080/15622975.2016.1190867

Bandelow, B., Wiltink, J., Alpers, G. W., Benecke, C., Deckert, J., Eckhardt-Henn, A., . . . Beutel, M. E. (2014). Deutsche S3-Leitlinie Behandlung von Angststörungen. Retrieved from www.awmf.org/leitlinien.html

Belvederi Murri, M., Prestia, D., Mondelli, V., Pariante, C., Patti, S., Olivieri, B., . . . Amore, M. (2016). The HPA axis in bipolar disorder: Systematic review and meta-analysis. *Psychoneuroendocrinology, 63*, 327-342. https://doi.org/10.1016/j.psyneuen.2015.10.014

Corona, G., Rastrelli, G., Morgentaler, A., Sforza, A., Mannucci, E., & Maggi, M. (2017). Meta-analysis of results of testosterone therapy on sexual function based on international index of erectile function scores. *European Urology, 72*(6), 1000-1011. https://doi.org/10.1016/j.eururo.2017.03.032

DGPPN, BÄK, KBV, AWMF, AkdÄ, BPtK, … DGRW (2015). *Unipolare Depression* (S3-Leitlinie/ Nationale VersorgungsLeitlinie, Version 5, 2nd ed.). Berlin, Germany: ÄZQ.

Ditzen, B., Schaer, M., Gabriel, B., Bodenmann, G., Ehlert, U., & Heinrichs, M. (2009). Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. *Biological Psychiatry, 65*(9), 728-731. https://doi.org/10.1016/j.biopsych.2008.10.011

Drobnjak, S., & Ehlert, U. (2011). Hunger- und Sättigungsregulation. In U. Ehlert & R. von Känel (Eds.), *Psychoendokrinologie und Psychoimmunologie* (pp. 151-162). Heidelberg, Germany: Springer.

Ehlert, U. (2011). Das endokrine System. In U. Ehlert & R. von Känel (Eds.), *Psychoendokrinologie und Psychoimmunologie* (pp. 3-36). Heidelberg, Germany: Springer.

Ehlert, U. (2013). Enduring psychobiological effects of childhood adversity. *Psychoneuroendocrinology, 38*(9), 1850-1857. https://doi.org/10.1016/j.psyneuen.2013.06.007

Ehlert, U., Gaab, J., & Heinrichs, M. (2001). Psychoneuroendocrinological contributions to the etiology of depression, posttraumatic stress disorder, and stress-related bodily disorders: The role of the hypothalamus-pituitary-adrenal axis. *Biological Psychology, 57*(1-3), 141-152. https://doi.org/10.1016/S0301-0511(01)00092-8

Elliott, J., Kelly, S. E., Millar, A. C., Peterson, J., Chen, L., Johnston, A., . . . Wells, G. A. (2017). Testosterone therapy in hypogonadal men: A systematic review and network meta-analysis. *BMJ Open, 7*(11), Article e015284.

Elraiyah, T., Sonbol, M. B., Wang, Z., Khairalseed, T., Asi, N., Undavalli, C., . . . Murad, M. H. (2014). Clinical review: The benefits and harms of systemic testosterone therapy in postmenopausal women with normal adrenal function: A systematic review and meta-analysis. *The Journal of Clinical Endocrinology & Metabolism, 99*(10), 3543-3550. https://doi.org/10.1210/jc.2014-2262

Fischer, S., & Cleare, A. J. (2017). Cortisol as a predictor of psychological therapy response in anxiety disorders: Systematic review and meta-analysis. *Journal of Anxiety Disorders, 47*, 60-68. https://doi.org/10.1016/j.janxdis.2017.02.007

Fischer, S., & Nater, U. M. (2015). Autonomes Nervensystem. In W. Rief & P. Henningsen (Eds.), *Psychosomatik und Verhaltensmedizin* (pp. 193-201). Stuttgart, Germany: Schattauer.

Fischer, S., Strawbridge, R., Herane Vives, A., & Cleare, A. J. (2017). Cortisol as a predictor of psychological therapy response in depressive disorders: Systematic review and meta-analysis. *The British Journal of Psychiatry, 210*(2), 105-109. https://doi.org/10.1192/bjp.bp.115.180653

Gordon, J. L., Rubinow, D. R., Eisenlohr-Moul, T. A., Leserman, J., & Girdler, S. S. (2016). Estradiol variability, stressful life events, and the emergence of depressive symptomatology during the menopausal transition. *Menopause, 23*(3), 257-266. https://doi.org/10.1097/GME.0000000000000528

Greenhalgh, A. M., Gonzalez-Blanco, L., Garcia-Rizo, C., Fernandez-Egea, E., Miller, B., Arroyo, M. B., & Kirkpatrick, B. (2017). Meta-analysis of glucose tolerance, insulin, and insulin resistance in antipsychotic-naive patients with nonaffective psychosis. *Schizophrenia Research, 179*, 57-63. https://doi.org/10.1016/j.schres.2016.09.026

Heim, C., Ehlert, U., & Hellhammer, D. H. (2000). The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology, 25*(1), 1-35. https://doi.org/10.1016/S0306-4530(99)00035-9

Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biological Psychiatry, 54*(12), 1389-1398. https://doi.org/10.1016/S0006-3223(03)00465-7

Ilyas, A., Hubel, C., Stahl, D., Stadler, M., Ismail, K., Breen, G., . . . Kan, C. (2018). The metabolic underpinning of eating disorders: A systematic review and meta-analysis of insulin sensitivity. *Molecular and Cellular Endocrinology*. Advance online publication. https://doi.org/10.1016/j.mce.2018.10.005

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., . . . Wang, P. (2010). Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. *The American Journal of Psychiatry, 167*(7), 748-751. https://doi.org/10.1176/appi.ajp.2010.09091379

Isidori, A. M., Buvat, J., Corona, G., Goldstein, I., Jannini, E. A., Lenzi, A., . . . Maggi, M. (2014). A critical analysis of the role of testosterone in erectile function: From pathophysiology to treatment-a systematic review. *European Urology, 65*(1), 99-112. https://doi.org/10.1016/j.eururo.2013.08.048

Jobst, A., Sabass, L., Hall, D., Brucklmeier, B., Buchheim, A., Hall, J., . . . Padberg, F. (2018). Oxytocin plasma levels predict the outcome of psychotherapy: A pilot study in chronic depression. *Journal of Affective Disorders, 227*, 206-213. https://doi.org/10.1016/j.jad.2017.10.037

Kan, C., Silva, N., Golden, S. H., Rajala, U., Timonen, M., Stahl, D., & Ismail, K. (2013). A systematic review and meta-analysis of the association between depression and insulin resistance. *Diabetes Care, 36*(2), 480-489. https://doi.org/10.2337/dc12-1442

Keech, B., Crowe, S., & Hocking, D. R. (2018). Intranasal oxytocin, social cognition and neurodevelopmental disorders: A meta-analysis. *Psychoneuroendocrinology, 87*, 9-19. https://doi.org/10.1016/j.psyneuen.2017.09.022

Kranz, T. M., Kopp, M., Waltes, R., Sachse, M., Duketis, E., Jarczok, T. A., . . . Chiocchetti, A. G. (2016). Meta-analysis and association of two common polymorphisms of the human oxytocin receptor gene in autism spectrum disorder. *Autism Research, 9*(10), 1036-1045. https://doi.org/10.1002/aur.1597

LoParo, D., & Waldman, I. D. (2015). The oxytocin receptor gene (OXTR) is associated with autism spectrum disorder: A meta-analysis. *Molecular Psychiatry, 20*(5), 640-646. https://doi.org/10.1038/mp.2014.77

Maletic, V., Eramo, A., Gwin, K., Offord, S. J., & Duffy, R. A. (2017). The role of norepinephrine and its alpha-adrenergic receptors in the pathophysiology and treatment of major depressive disorder and schizophrenia: A systematic review. *Frontiers in Psychiatry, 8*, Article 42. https://doi.org/10.3389/fpsyt.2017.00042

Marsh, W. K., Bromberger, J. T., Crawford, S. L., Leung, K., Kravitz, H. M., Randolph, J. F., . . . Soares, C. N. (2017). Lifelong estradiol exposure and risk of depressive symptoms during the transition to menopause and postmenopause. *Menopause, 24*(12), 1351-1359. https://doi.org/10.1097/GME.0000000000000929

Melcangi, R. C., Giatti, S., & Garcia-Segura, L. M. (2016). Levels and actions of neuroactive steroids in the nervous system under physiological and pathological conditions: Sex-specific features. *Neuroscience & Biobehavioral Reviews, 67*, 25-40. https://doi.org/10.1016/j.neubiorev.2015.09.023

Meuret, A. E., Rosenfield, D., Bhaskara, L., Auchus, R., Liberzon, I., Ritz, T., & Abelson, J. L. (2016). Timing matters: Endogenous cortisol mediates benefits from early-day psychotherapy. *Psychoneuroendocrinology, 74*, 197-202. https://doi.org/10.1016/j.psyneuen.2016.09.008

Meyer-Lindenberg, A., Domes, G., Kirsch, P., & Heinrichs, M. (2011). Oxytocin and vasopressin in the human brain: Social neuropeptides for translational medicine. *Nature Reviews Neuroscience, 12*(9), 524-538. https://doi.org/10.1038/nrn3044

Morris, M. C., Compas, B. E., & Garber, J. (2012). Relations among posttraumatic stress disorder, comorbid major depression, and HPA function: A systematic review and meta-analysis. *Clinical Psychology Review, 32*(4), 301-315. https://doi.org/10.1016/j.cpr.2012.02.002

Nastri, C. O., Lara, L. A., Ferriani, R. A., Rosa, E. S. A. C., Figueiredo, J. B., & Martins, W. P. (2013). Hormone therapy for sexual function in perimenopausal and postmenopausal women. *Cochrane Database of Systematic Reviews,* 6, Article CD009672.

Nater, U. M., Fischer, S., & Ehlert, U. (2011). Stress as a pathophysiological factor in functional somatic syndromes. *Current Psychiatry Reviews, 7*(2), 152-169. https://doi.org/10.2174/157340011796391184

Nater, U. M., & Rohleder, N. (2009). Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: Current state of research. *Psychoneuroendocrinology, 34*(4), 486-496. https://doi.org/10.1016/j.psyneuen.2009.01.014

Pillinger, T., Beck, K., Gobjila, C., Donocik, J. G., Jauhar, S., & Howes, O. D. (2017). Impaired glucose homeostasis in first-episode schizophrenia: A systematic review and meta-analysis. *JAMA Psychiatry, 74*(3), 261-269. https://doi.org/10.1001/jamapsychiatry.2016.3803

Prince, A. C., Brooks, S. J., Stahl, D., & Treasure, J. (2009). Systematic review and meta-analysis of the baseline concentrations and physiologic responses of gut hormones to food in eating disorders. *The American Journal of Clinical Nutrition, 89*(3), 755-765. https://doi.org/10.3945/ajcn.2008.27056

Ricken, R., Bopp, S., Schlattmann, P., Himmerich, H., Bschor, T., Richter, C., . . . Adli, M. (2017). Ghrelin serum concentrations are associated with treatment response during lithium augmentation of antidepressants. *International Journal of Neuropsychopharmacology, 20*(9), 692-697. https://doi.org/10.1093/ijnp/pyw082

Ricken, R., Bopp, S., Schlattmann, P., Himmerich, H., Bschor, T., Richter, C., . . . Adli, M. (2016). Leptin serum concentrations are associated with weight gain during lithium augmentation. *Psychoneuroendocrinology, 71*, 31-35. https://doi.org/10.1016/j.psyneuen.2016.04.013

Rutigliano, G., Rocchetti, M., Paloyelis, Y., Gilleen, J., Sardella, A., Cappucciati, M., . . . Fusar-Poli, P. (2016). Peripheral oxytocin and vasopressin: Biomarkers of psychiatric disorders? A comprehensive systematic review and preliminary meta-analysis. *Psychiatry Research, 241*, 207-220. https://doi.org/10.1016/j.psychres.2016.04.117

Salzmann, S., Euteneuer, F., Laferton, J. A. C., Auer, C. J., Shedden-Mora, M. C., Schedlowski, M., . . . Rief, W. (2017). Effects of preoperative psychological interventions on catecholamine and cortisol levels after surgery in coronary artery bypass graft patients: the randomized controlled PSY-HEART trial. *Psychosomatic Medicine, 79*(7), 806-814. https://doi.org/10.1097/PSY.0000000000000483

Soria, V., Gonzalez-Rodriguez, A., Huerta-Ramos, E., Usall, J., Cobo, J., Bioque, M., . . . Labad, J. (2018). Targeting hypothalamic-pituitary-adrenal axis hormones and sex steroids for improving cognition in major mood disorders and schizophrenia: A systematic review and narrative synthesis. *Psychoneuroendocrinology, 93*, 8-19. https://doi.org/10.1016/j.psyneuen.2018.04.012

Stetler, C., & Miller, G. E. (2011). Depression and hypothalamic-pituitary-adrenal activation: A quantitative summary of four decades of research. *Psychosomatic Medicine, 73*(2), 114-126. https://doi.org/10.1097/PSY.0b013e31820ad12b

Stubbs, B., Wang, A. K., Vancampfort, D., & Miller, B. J. (2016). Are leptin levels increased among people with schizophrenia versus controls? A systematic review and comparative meta-analysis. *Psychoneuroendocrinology, 63*, 144-154. https://doi.org/10.1016/j.psyneuen.2015.09.026

Tak, L. M., Cleare, A. J., Ormel, J., Manoharan, A., Kok, I. C., Wessely, S., & Rosmalen, J. G. M. (2011). Meta-analysis and meta-regression of hypothalamic-pituitary-adrenal axis activity in functional somatic disorders. *Biological Psychiatry, 87*(2), 183-194. https://doi.org/10.1016/j.biopsycho.2011.02.002

Valstad, M., Alvares, G. A., Egknud, M., Matziorinis, A. M., Andreassen, O. A., Westlye, L. T., & Quintana, D. S. (2017). The correlation between central and peripheral oxytocin concentrations:

A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews, 78*, 117-124. https://doi.org/10.1016/j.neubiorev.2017.04.017

Wolf, J. M., & Saucier, E. (2013). *Psychoneuroendocrinology.* In M. D. Gellman & J. R. Turner (Eds.), *Encyclopedia of Behavioral Medicine.* New York, NY, USA: Springer. https://doi.org/10.1007/978-1-4419-1005-9

Zilcha-Mano, S., Porat, Y., Dolev, T., & Shamay-Tsoory, S. (2018). Oxytocin as a neurobiological marker of ruptures in the working alliance. *Psychotherapy and Psychosomatics, 87*(2), 126-127. https://doi.org/10.1159/000487190

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Evidence-Based Psychodynamic Therapies for the Treatment of Patients With Borderline Personality Disorder

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Abstract

Background: Borderline Personality Disorder (BPD) is a serious health issue associated with a high burden for the individual and society. Among the "Big Four" of evidence-based treatments for patients with BPD are two psychodynamic therapies that have evolved from classic psychoanalytic treatment with a change of setting and change of focus: Transference-Focused Psychotherapy (TFP) and Mentalization-Based Treatment (MBT).
Aims: This overview provides a comparison of the two treatments in terms of stance, clinical concepts, costs and key interventions. Furthermore, the current literature on the efficacy of both treatments is reviewed.
Results: While TFP focuses on the content of disintegrated representations of self and other, MBT focuses on the processing of mental states. Both treatments diverge in their clinical concepts and interventions for the treatment of BPD.
Conclusion: Although both treatments are regarded as effective in treating BPD, no direct comparison of both treatments has been made so far. Future studies are needed to investigate mechanisms of change and derive recommendations for a differential indication.

Keywords

psychodynamic psychotherapy, borderline personality disorder, mentalization-based treatment, transference-focused psychotherapy, efficacy, clinical concepts

Highlights

- Specialized therapies for BPD have favorable drop-out rates and outcome compared to non-specialized ones.
- MBT and TFP have very diverse clinical concepts and interventions for the treatment of BPD.
- Both, MBT and TFP show efficacy in RCTs.
- No trial has directly compared MBT and TFP; there is no evidence base for differential indication.

The Cochrane review (Stoffers et al., 2012) on psychological therapies for Borderline Personality Disorder (BPD) lists several approaches as 'probably effective' in treating BPD. Four psychological treatments are described as evidence-based, the "Big Four". Among those two psychodynamic treatments are listed: Mentalization-Based Therapy (MBT) and Transference-Focused Psychotherapy (TFP). Both represent the trend in psychodynamic therapies to develop disorder-specific treatments that can be tested for efficacy in contrast to a classic, more transdiagnostic approach. Furthermore, psychodynamic therapies have been developed that deviate from the classic Freudian conceptualizations of addressing unconscious conflict to improving personality functioning instead. In this paper, we will outline these current developments of psychodynamic treatments among the "Big Four" for BPD as the most prevalent disorder in clinical settings (Torgersen, 2005), due to a lack of trials for other psychodynamic approaches (e.g. Dynamic Deconstructive Psychotherapy or Psychoanalytic Interactional Method). First, we will summarize the common ground of psychodynamic therapies and, secondly, describe the clinical and change theory as well as therapeutic stance and key interventions of the two treatments. In a third step, TFP and MBT will be compared and contrasted with regard to their similarities and differences. The paper concludes with a summary of the current research findings on the efficacy of MBT and TFP for BPD and points out future directions for clinical research of these two approaches. Differences in efficacy to classic psychodynamic treatment will be discussed.

Common Features of Psychodynamic Psychotherapy

The term psychodynamic psychotherapy was established to describe therapies following the core psychoanalytic principles but with a lower weekly session rate and using a face-to-face setting instead of the classic Freudian couch setting (Whitehorn, Braceland, Lippard, & Malamud, 1953). Furthermore, psychodynamic psychotherapies establish a treatment focus and limit treatment goals also with regard to symptomatic changes. Par-

allel to the development of psychodynamic psychotherapy, clinical theories were broadened from seeing symptoms not only as a manifestation of unconscious conflicts but also as impairments in personality functioning and disturbed relationships (OPD-2, OPD Taskforce, 2008). Following the demands of evidence-based medicine, disorder-specific treatment manuals were established, e.g. for the treatment of panic disorders (Milrod et al., 2007) and depression (Lemma, Target, & Fonagy, 2011). The core ideas of psychodynamic therapies remained the following (Shedler, 2010):

1. Focus on emotions and affect
2. Exploration of aspects that patients tend to avoid (e.g. painful and threatening aspects of experience), which is called defense or resistance in psychoanalytic terms
3. Identification of recurrent topics or themes with regard to self, other, relationships, etc.
4. Discussion of past experiences that help to contextualize current experiences
5. Focus on relationships, especially the therapeutic relationship
6. Exploration of dreams, phantasies and wishes

All of these aspects can also be found in MBT and TFP; however, there is a shift of focus in the treatment of BPD to emphasize the "here-and-now" instead of discussing past events. Both treatments work very explicitly with the current therapeutic relationship and the exploration of dreams, phantasies and wishes is not central for the therapeutic process, at least at the beginning of treatment. Furthermore, psychodynamic therapies follow the goal to change distorted representations of self, other or relationships in a quite comparable way to Cognitive-Behavioral Therapy (CBT). These can be distinguished at the level of intervention: while CBT aims to change patients' dysfunctional beliefs at a micro level, psychodynamic therapies reach out to change personality aspects e.g. with regard to depression at a macro level (Luyten, Blatt, & Fonagy, 2013). Both aim to change the *content* of representations. However, because a large number of patients do not correspond to a treatment approach focusing on the content of representations, recently in both therapeutic schools, new therapies have been developed that shift from addressing content to the *processing* of mental states itself (e.g. *how* we think and interpret instead of *what* we think). In this paper, we will regard TFP as a primarily content-focused treatment, whereas MBT focuses more on the processing of mental states, which can be regarded in line with the third wave therapies in CBT. Before comparing these two specific treatment approaches- TFP and MBT-, we will summarize the core symptoms and burden of BPD.

Borderline Personality Disorder

BPD is a severe health issue characterized by at least five of the following nine criteria (Diagnostic and Statistical Manual of Mental Disorders [5th ed.; DSM–5]; American Psychiatric Association, 2013): a) unstable relationships, b) inappropriate anger, c) frantic effort to avoid abandonment, d) affective instability, e) impulsivity, f) self-harm/suicidality, g) dysphoria, h) stress-related paranoid thoughts and i) identity disturbance and dissociation. Point prevalence in community samples ranges from 0.7-3.9% (Trull, Jahng, Tomko, Wood, & Sher, 2010), lifetime prevalence is around 6% (Grant et al., 2008). In a recent meta-analysis with n = 66,914 included individuals from community samples of 9 studies in Western countries the prevalence rate was 1.90% (Volkert, Gablonski, & Rabung, 2018). Furthermore, BPD is the most common personality disorder in clinical populations, with prevalence rates of around 10% in outpatient and 15-25% in inpatient settings (Torgersen, 2005). BPD is often associated with both comorbid axis I and II disorders: approx. 85% of BPD patients have a 12-months diagnosis of at least one axis I and 74% for another axis II disorder (Grant et al., 2008). 69-80% of BPD patients engage in suicidal behavior and 3-10% commit suicide with a 50 fold heightened risk in comparison to the general population (Gunderson, Weinberg, & Choi-Kain, 2013; Leichsenring, Leibing, Kruse, New, & Leweke, 2011; Oldham, 2006). BPD accounts for 2.2% of all disability adjusted life years (DALYs), 1.2% of all DALYs (ranking 3rd in mental disorders in women, and 4th in men) and suicide accounts for 1.0-2.8% of all DALYs (Victorian Government Department of Human Services, 2005). The burden of BPD on society in terms of productivity losses and other indirect costs is assumed to reach 76.3% of the total costs (Olesen, Gustavsson, Svensson, Wittchen, & Jönsson, 2012). Similarly, direct costs of BDP are considered to be higher than in depression or diabetes (Wagner et al., 2013), with average per capita costs ranging between 11,000€ and 14,000€ (Salvador-Carulla et al., 2014) per year. In sum, BPD is a severe treatment condition that comes with a high burden for the individual and society. However, treatment of BPD patients is emotionally challenging for therapists, and therapists often decline treatment with this group of patients; although 50% of therapists agree that a BPD-specific treatment qualification is useful, only 3% have such a qualification (Jobst, Hörz, Birkhofer, Martius, & Rentrop, 2010). Thus, there is a high need of training therapists in BPD-specific treatment approaches. The two approaches that will be presented here, MBT (Bateman & Fonagy, 2016) and TFP (Yeomans, Clarkin, & Kernberg, 2015), offer an additional training on top of a psychodynamic (or other) psychotherapeutic training that was created to treat BPD more effectively.

A Content-Focused Psychodynamic Treatment – Transference Focused Psychotherapy

TFP was developed by Frank Yeomans, John Clarkin, and Otto Kernberg (Yeomans et al., 2015) and is associated with a new conceptual idea of identity formation and personality organization. The aim of treatment is to decrease the symptomatic burden and interpersonal problems in patients with BPD by changing patients' mental representations of others and self that underlies their behavior (Clarkin, Cain, & Lenzenweger, 2018), to meaningfully improve functioning in the domains of work, studies and profession, and intimate relations (Yeomans et al., 2015).

Clinical Concept

Personality organization is described as comprising three aspects of personality functioning: identity integration, level of defense mechanisms and degree of reality testing. Following Kernberg (1967), Borderline personality organization is marked by identity diffusion, low level of defenses but mainly intact reality testing. Thereby, identity diffusion is considered central to the clinical understanding of BPD in TFP and is related to a lack of coherence in the individual's experience and understanding of both self and others. Furthermore, social signals are consistently misunderstood because the inner experience of a BPD patient is dominated by aggressive internalized object relations that are split from idealized ones. Thus, identity diffusion is associated with defensive strategies involving dissociation of conscious aspects of conflicting experiences (splitting). The lack of an integrated self is also seen as leading to internal distress and emptiness that lead to patients' attempts to relieve distress through impulsive acting out (Kernberg, 1967). Kernberg's etiology follows the idea of object relation theory that early experiences of self and others are organized by splitting, meaning that positive and negative representations of self and other need to be gradually integrated to achieve normal functioning. In BPD, positive and negative representations of self and other remain separated/ disintegrated because negative representations contain traumatic affects that would possibly destroy positive representations.

Change Theory

The authors propose that TFP helps patients to establish an increased affect regulation achieved through the growing ability of the patient to psychologically reflect and integrate thoughts, emotions and behavior and to establish positive relationships with others (Kernberg, 2016). This is achieved through a modification of personality structure by linking the dissociated parts of positive and negative representations that are enacted in the therapeutic relationship. The patient's partial representations are experienced in the therapeutic relationship that mirror splitting in the patient (transference). This can lead to a rapid change in the therapeutic relationship, e.g. an idealization of the therapist fol-

lowed by a fear of being dominated or threatened, which is outside of the patient's awareness. The therapist describes these different states of the relationship and links this with the inner experience of the patient. This way an integration of the split off idealized and persecutory segments of experience can take place, i.e. identity diffusion can be resolved. By addressing the different split-off representations of self and other the therapist engages the patient in thinking and reflecting about their emotional responses and behavior and links this, moment by moment, to the experiences in the therapeutic relationship. This leads to a reflection in the here and now with another person and a growing awareness of how the perception of others is distorted by expectations derived from internal representations. Within this therapeutic process the patient's view of current interpersonal realities becomes more accurate.

Setting

TFP begins with a verbal contract that serves as a framework to discuss risks to a patient's life (suicidality, self-harm, drug abuse) as well as behavior that potentially limits or hinders the continuation of therapy (leaving a job, insurance, moving to another city). Furthermore, the contract aims at reducing any gains that the patient would take from their symptoms with regard to negative reinforcements. After having agreed on a common contract, two individual sessions weekly are carried out with weekly supervision. The average treatment duration is between two and three years.

Stance

The therapist takes a more active stance in comparison to classic psychoanalytic treatment by paying more attention to the external reality of the patient (e.g. breaking the contract, antisocial behavior) and selects priority themes that need to be addressed in every session in the material the patient is presenting. The stance is characterized by the "technical neutrality", focusing on the "here-and-now" as well as balancing between exploring and confronting the patient with incompatible views on the one hand and regulation of arousal on the other hand. Technical neutrality describes the general stance of continuously keeping the goal of therapy in mind with an attitude of objective inquiry, to clarify issues without being judgmental. Contradictions in the patient's perception or representations of self and others are observed at three levels: what the patient is saying, how the patient is acting (inside and outside session) as well as the counter-reactions and feelings of the therapist. The latter requires constant monitoring of what belongs to the patient, the therapist and/or their interaction.

Key Interventions

While the patient is asked to freely associate and disclose any idea that comes to mind, the therapist listens carefully and uses the three following interventions: clarification,

confrontation and interpretation. Clarification means to thoroughly explore the patient's subjective experience with a special focus on contradictions or conflicts as well as affects in his/her perception of self and others. This intervention aims to promote mentalization of internal states (Yeomans, Levy, & Caligor, 2013). Confrontations take the therapeutic work to the second level of actively pointing out discrepancies between the three channels of communication (verbal, non-verbal and counter-reactions of the therapist) (Zerbo, Cohen, Bielska, & Caligor, 2013). Finally, interpretations aim to integrate contradictions by offering a hypothesis for a deeper understanding of the different self and other representations that dominate the patient's thinking and feeling in relationships. In the beginning and middle parts of the treatment, TFP recommends to avoid so-called genetic interpretations that link childhood experiences to current states of mind but stay in the here-and-now.

Time and Costs

Training comprises 34 weekly seminars over a duration of one year including supervision. This is followed by 6 months' home study and supervision. The cost of the training adds up to 3,000€ (TFP Institute Munich, Germany). Treatment costs for an individual patient may vary from country to country. Number, duration and frequency of therapeutic sessions may approximately range from a minimum of 180 hours (two weekly sessions for one year) to a maximum of 405 sessions (three sessions weekly for three years) based on data from trial therapies. A cost effectiveness study revealed average costs for TFP at about 46.000€ and concluded that SF was more cost-effective in comparison to TFP (van Asselt et al., 2008). However, there is no time-limitation to TFP according to the manual, which makes cost calculation outside of research difficult.

Widening Scope (Disorders and Age Groups)

TFP started to provide an adapted and manualized psychoanalytic treatment for BPD, and there are further adaptions for the treatment of adolescents with Borderline features (TFP-Adolescence, Normandin, Ensink, Yeomans, & Kernberg, 2014; Adolescent Identity Treatment, Foelsch et al., 2014) and other personality disorders such as Narcissistic Personality Disorder. Furthermore, the treatment approach was adapted for implementation in an acute psychiatric setting (Zerbo et al., 2013).

A Process-Focused Psychodynamic Treatment – Mentalization-Based Treatment

MBT is a manualized treatment protocol developed by Anthony Bateman and Peter Fonagy (Bateman & Fonagy, 2016). The treatment is based on validating the emotional experience of patients within a significant therapeutic relationship and promotes several tech-

niques that directly aim to stabilize or enhance mentalizing (Bateman & Fonagy, 2016). Mentalization is the imaginative ability to interpret human behavior in terms of mental states (Fonagy, Gergely, Jurist, & Target, 2002). Empirical research has shown that although social cognition is not necessarily impaired in BPD the construct of understanding others in emotionally intense relationships is highly impaired in BPD, which may underlie the core problems of these patients (Fonagy, Luyten, & Strathearn, 2011). By promoting mentalizing, MBT addresses the interpersonal sensitivity in BPD.

Clinical Concept

Effective mentalizing is characterized by a genuine curiosity about mental states' underlying behavior, a flexibility in interpreting self and others as well as the knowledge that mentalizing is inaccurate most of the time and needs communication with others to clarify intentions more precisely. Furthermore, healthy mentalizing enables an individual to actively shift between different poles of mentalizing, e.g. self vs. others, integration of cognition and affect or implicit vs. explicit mentalizing. Patients with BPD are often overwhelmed by their emotions, make over-quick assumptions and focus on thinking about others with fears of abandonment and rejection. In MBT, the prototypical problems for working with patients with BPD are regarded as a sign of vulnerability in mentalizing that goes along with a high interpersonal sensitivity. An attachment threat leads to a breakdown in mentalizing, which leads to a failure of affect regulation and impulsive behavior. The vulnerability in mentalizing has been conceptualized as three different forms of inadequate mentalizing: teleological mode, psychic equivalence and pseudo-mentalizing. Teleological thinking overgeneralizes behavior as proof for internal states, whereas psychic equivalence generalizes from internal experience to the external reality. Pseudo-mentalizing creates mental theories without a connection between internal and external experience.

Change Theory

The proposed mechanism of change in MBT is to stabilize mentalizing in certain focus areas to create a psychic buffer between affect and behavior to foster affect regulation, reduce impulsivity and promote functional supportive relationships. This is reached by employing "contrary moves" to create more flexibility in using the different poles of mentalizing. If the patient is stuck in thinking about the self, the therapist will try to shift him or her towards thinking about others. If the patient is too certain about quickly made assumptions, the therapist will try to slow down and question the first assumption, etc. By sharing or disclosing the therapist's interpersonal experience with the patient from the beginning and throughout the process, the patient can find him/herself in the mind of the therapist and reflect on how the therapist is represented in the mind of the patient. Using constant empathic validation of the patient's affects and working slowly on cur-

rent experiences with the therapist and other important others; the patient develops epistemic trust and is able to generalize helpful mentalizing experiences with the therapist to other relationships outside of therapy. Furthermore, by sharing a written case formulation, the patient learns about the therapist's idea of the patient's mentalizing failures and help him/her to establish more agency and responsibility for his/her behavior with regard to core symptoms e.g. self-harm, drug abuse.

Setting

MBT was initially developed as an inpatient treatment with a duration of 18 months and evolved to an intensive outpatient program that is now commonly limited to 12 months. MBT sets off with a diagnostic phase. In addition to standard diagnostic assessment, the clinician is assessing mentalizing problems and interpersonal triggers that are associated with the core problem behavior. This is written down in a case formulation that summarizes the clinician's current understanding of the patient's vulnerabilities and mentalizing problems all set in the context of current relationships and behavior. The case formulation is shared with the patient, serves as a focus for treatment, and is revised approx. every three months. In addition to the case formulation, a crisis plan is developed together with the patient entailing information which the patient finds helpful or hindering during breakdowns for him/herself, professionals and significant others. After the diagnostic phase the patient participates in a psycho-education group that teaches core elements of the treatment including an understanding of the BPD diagnosis. After 12 sessions the group changes its format to a MBT-group therapy focusing on elaborating perspectives from each group member. Parallel to the weekly group sessions patients have one weekly individual session.

Stance

Several aspects are essential for the MBT stance: being curious and enthusiastic for mental states, being authentic, empathic and validating as well as most importantly, taking a not-knowing stance. The latter is based on the modesty that no one can read minds and creates a less hierarchical relationship between therapist and patients. The therapist is not the expert for the patient's mind but rather takes an inquisitive stance to explore together with the patient what kind of thinking is helpful or unhelpful to have good relationships with others. Another focus is related to misunderstanding each other. Misunderstanding is considered as an opportunity to learn about perceptions, interpretations and experience. The therapist actively structures the session by focusing on topics related to the case formulation, management of arousal and monitoring the level of mentalizing.

Key Interventions

Interventions start from the surface and work towards relational mentalizing of the therapeutic relationship if the current arousal and level of mentalizing allows. During times of high arousal it is recommended to intervene supportively by empathically validating the patient's subjective experience and addressing non-mentalizing by exploring affects, certainties, quick assumptions, and by challenging pseudo-mentalizing. The techniques are called "stop and stand" or "stop, rewind and explore" that slow down the processing of current experiences. Lower levels of arousal allow to start basic mentalizing around the focus of treatment such as triggers of strong affects and effect on behavior and others as well as linking different experiences to patterns of experience. Finally, exploring the current affect during the session (affect focus) and the relationship between therapist and patient are seen as crucial change mechanisms as this allows an understanding of interpersonal processes in the here-and-now. MBT deviates from classic psychoanalytic interpretations as this is regarded aversive for BPD patients. Thus, within the MBT framework it is recommended to contextualize affects and patterns of behavior in the here-and-now that should not be interpreted as a mere repetition of past relationships and experiences.

Time and Costs

Training comprises 5 days and four supervised cases with at least 24 sessions each and four sessions of supervision per case. Supervision and training add up to an overall cost of 1,600€ when following the requirements of the Anna-Freud-Centre in London but may vary country wise. Number, duration and frequency of MBT sessions based on one weekly group and one individual session ranges between 90 sessions in twelve months or 120 sessions in 18 months. MBT was originally developed as an inpatient treatment, which is more costly than the outpatient program. However, exact numbers have not been reported yet. A recent RCT in the Netherlands tested the efficacy between MBT outpatient and day-hospital, and reported a superiority in secondary outcomes for the more costly day-hospital treatment (Smits et al., 2019). Cost-effectiveness data comparing both settings is not available yet.

Widening Scope (Disorders and Age Groups)

Meanwhile, programs have been developed for adolescents with BPD (MBT-A), parents with BPD (MBT-Lighthouse), Conduct Disorder, Antisocial Personality Disorder, Eating Disorders, families (MBT-F), children (MBT-C) and hard to reach clients (AMBIT) (for an overview: Bateman & Fonagy, 2019).

Efficacy of PD Treatments for BPD

Efficacy of TFP

Three RCTs have demonstrated the efficacy of TFP. The first efficacy trial was conducted by Giesen-Bloo et al. (2006), with outpatients (n = 88) comparing TFP with Schema-Focused Therapy (SFT) with 2 weekly sessions over a duration of 3 years. Using an intention-to-treat approach, statistically and clinically significant improvements were found for both treatments on all measures after 1-, 2-, and 3-year treatment periods. However, SFT patients had a lower risk for drop-out (RR = 0.52) and after 3 years of treatment, survival analyses demonstrated that significantly more SFT patients recovered or showed reliable clinical improvement. Robust analysis of covariance (ANCOVA) showed that they also improved more in general psychopathologic dysfunction and showed greater increases in quality of life. Arntz, Stupar-Rutenfrans, Bloo, van Dyck, and Spinhoven (2015) reanalyzed the Giessen-Bloo study and identified the following predictors for drop-out and reduced recovery: initial burden of dissociation, hostility and childhood physical abuse, whereby in-session dissociation (observer-report) was identified as a mediator. Another outpatient RCT with n = 90 patients was conducted by Clarkin, Levy, Lenzenweger, and Kernberg (2007), who compared TFP (two individual weekly sessions) with DBT (weekly individual + group plus telephone consultation) and Dynamic Supportive Treatment (DST) (one individual weekly session) over a duration of 12 months. They found significant improvement for all three treatments on a number of outcomes: depression, anxiety, global functioning and social adjustment. No differences were found between the three different treatments; only TFP had a two times lower risk of drop-out (compare also Oud, Arntz, Hermens, Verhoef, & Kendall, 2018, for a summary). Thereby individual slopes differed with regard to within-patient effects. Individual growth curve analysis showed that DBT and TFP had significant change rates compared to DST on suicidality, whereas TFP and DST had significant change rates compared to DBT on anger and impulsivity. Furthermore, only TFP showed significant change rates in aggression (direct and verbal assault) and irritability. Doering et al. (2010) investigated the efficacy of a TFP treatment compared to community treatment by experts (CTBE) over one year in n = 104 female patients with BPD. In this trial, TFP showed superiority to CTBE with regard to reduced drop-out (38.5% v. 67.3%), suicide attempts, borderline symptomatology, increased psychosocial functioning, personality organization and psychiatric inpatient admissions. No differences between the two treatment conditions were observed for depression, anxiety and general psychopathology. However, self-harming behavior did not change in either group. In a further analysis of the same data by Fischer-Kern et al. (2015) significant improvements in reflective functioning was also found for the TFP vs. the TAU group with a medium between-group effect size (d = 0.45).

Efficacy of MBT

Four RCTs have investigated the efficacy of MBT in comparison to psychiatric services (Bateman & Fonagy, 1999), structured clinical services including supportive psychotherapy (Bateman & Fonagy, 2009; Jørgensen et al., 2013) and in adolescents with non-suicidal self-injury (NSSI), who mainly fulfilled criteria for BPD (Rossouw & Fonagy, 2012). MBT proved to be superior to TAU/ clinical management in NSSI, suicide attempts, psychiatric symptoms, and hospitalization (Bateman & Fonagy, 1999, 2009; Rossouw & Fonagy, 2012) as well as core BPD symptoms (Bales et al., 2012; Rossouw & Fonagy, 2012). One independent RCT confirmed positive effects for MBT in comparison to supportive therapy for general functioning, suggesting that MBT may address core problems in BPD beyond NSSI and suicidality (Jørgensen et al., 2013). MBT is the only treatment for which superiority to clinical management was demonstrated in all primary outcome variables as well as achieving significantly higher levels of employment or academic/occupation training eight years after admission (Bateman & Fonagy, 2008). Findings also demonstrate that MBT shows superiority over TAU for interpersonal problems and general functioning (Stoffers et al., 2012). In sum, MBT has demonstrated reliable improvements for psychiatric symptoms. A mediator analysis in an adolescent trial demonstrated that two changing variables were partially explaining differences in outcome between control and intervention group. These variables were changes in mentalizing and attachment avoidance, which were specific to the MBT effects (Rossouw & Fonagy, 2012). In a recent naturalistic study with a sample of 175 patients with BPD treated in an inpatient setting, changes of mentalizing operationalized with the Reflective Functioning Questionnaire Uncertainty Scale (RFQ) were significantly associated with changes in outcome (r = .89) (De Meulemeester, Vansteelandt, Luyten, & Lowyck, 2018). This can be regarded as first evidence for a proposed specific change mechanism, i.e. changes in mentalizing mediate symptom improvement in BPD.

Reviews and Meta-Analyses

Seven systematic reviews on the general efficacy of psychological therapies for BPD (Brazier et al., 2006; Cristea et al., 2017; Juanmartí & Lizeretti, 2017; Leichsenring et al., 2011; Oud et al., 2018; Stoffers et al., 2012) and therapy retention have been conducted, respectively (Barnicot, Katsakou, Marougka, & Priebe, 2011). The Cochrane review (Stoffers et al., 2012) lists several approaches as 'probably effective' in treating BPD. Among those treatment approaches, MBT is the most frequently investigated after DBT. The authors recommend to conduct future trials with more than one psychological treatment and to include quality of life and preference measures across different programs.

In a recent meta-analysis investigating RCTs on psychotherapy efficacy in reducing suicidal attempts and NSSI (Calati & Courtet, 2016), efficacy was established only for MBT compared to DBT, CBT, Cognitive Therapy and Interpersonal Psychotherapy. How-

ever, results were based on the inclusion of only two MBT RCTs. In an updated meta-analysis, Cristea et al. (2017) with k = 33 studies (n = 2,256 patients) conclude that only DBT and psychodynamic approaches were more effective than control interventions, however risk of bias was a significant moderator and publication bias was persistent particularly at follow-up. McLaughlin, Barkowski, Burlingame, Strauss, and Rosendahl (2019) investigate in k = 24 RCTs with over n = 1,500 patients the efficacy of group psychotherapy for BPD and find that group psychotherapy has a large effect on the reduction of BPD symptoms and a moderate effect on suicidality/ parasuicidal symptoms. While the largest numbers of studies available have investigated DBT, theoretical orientation of treatment was not a significant moderator for BPD symptoms in this meta-analysis. McLaughlin et al. (2019) conclude that dismantling studies, investigating the effect of various treatment components are promising. Leichsenring et al. (2011) and the Cochrane review (Stoffers et al., 2012) criticize the low study quality across BPD trials due to researcher allegiance, attention bias and small samples. They conclude that there is a strong need for confirmatory trials with high study quality and sufficient sample sizes.

Oud et al. (2018) summarize in their review and meta-analysis RCTs on DBT, MBT, TFP and ST to compare specialized therapies for BPDs with non-specialized treatments. When pooling comparison data from specialized treatments vs. community treatment by experts, they demonstrate that specialized psychodynamic treatments like MBT or TFP are superior to non-specialized psychodynamic treatment with regard to overall BPD severity and drop-out. With regard to self-injury TFP showed no superiority and with regard to suicidality both DBT and TFP were no better than community expert therapists. However, these results have to be interpreted cautiously as they are based on three trials only.

Similarities and Differences Between MBT and TFP

Both treatment approaches are regarded as evidence-based and are gathering further proof in ongoing trials. So far, mechanisms of change have not been empirically established; however, this is, unfortunately, currently the case for all psychotherapies. As no study has directly compared TFP and MBT so far, it is unclear if one is more effective than the other or more suited for BPD and respective subgroups. Thus, a differential indication for the treatment of patients with BPD cannot be made based on empirical findings. There is no evidence that allows to choose which psychotherapy may be the most appropriate for which patient profile (Fonagy, Luyten, & Bateman, 2017). Aside from BPD, the widening scope of treating other personality disorders reveals recommendations for treating patients with internalizing personality disorders with TFP (e.g. Narcissistic PD) (Kernberg, 2016) and patients with externalizing personality disorders with MBT (e.g. ASPD) (Bateman, O'Connell, Lorenzini, Gardner, & Fonagy, 2016).

TFP and MBT are based on different clinical and theories of change. TFP is more stringently rooted in classic psychoanalytic theory and jargon, while MBT created a new conceptual framework by bridging several theoretical underpinnings from psychoanalysis, attachment theory and general developmental psychology. Differences can also be found with regard to the setting: while TFP deviates from classic psychoanalysis only by not using the couch and reducing the weekly frequency to one to two hours, MBT has integrated psycho-education and group therapy which may create less pressure or intensity. However, the dyadic therapeutic work itself appears quite similar even though both approaches use different terminology for their interventions. Especially, clarification and confrontation in TFP are very close to exploration, clarification and challenge in MBT. Furthermore, establishing a contract and crisis plan at the beginning of therapy, working in the here-and-now, using the therapeutic relationship as a training ground and monitoring the therapist's counter-reaction is required in both therapies.

Major differences can be found in the general therapeutic stance that each approach is advocating. A TFP therapist is asked to remain in technical neutrality (not taking a stance towards or against any content discussed). On the contrary, the MBT therapist is asked to be enthusiastic and praising for mentalizing as well as disclosing his/her emotions if this is regarded as helpful to create a mentalizing process. While TFP is deploying a content-focused approach taking an interpretative expressive therapeutic stance, MBT focuses on the process of thinking about mental states based on a supportive therapeutic stance. Yet again, there is also a considerable overlap: Interestingly, TFP also increases mentalizing (Fischer-Kern et al., 2015; Levy et al., 2006), which may be evidence that the core therapeutic work of clarification and confrontation and maybe also interpretation creates robust mentalizing. As mechanism of change studies in MBT reveal that increasing reflective thinking is indeed mediating symptomatic improvement in BPD, this could also be interpreted as a common change factor across treatments in BPD (Goodman, 2013). Hence, it would be worth investigating these specific differences and similarities in process research as well as within non-inferiority trials to test the efficacy.

Dissemination of MBT and TFP is a major challenge as many psychodynamic therapists are skeptical towards disorder-specific treatment and variations from a highly individualized and transdiagnostic approach that is typical for psychodynamic therapies (Gonzalez-Torres, 2018). Furthermore, accredited supervisors and trainers are still scarce for both TFP and MBT, and this significantly hinders the international dissemination of training programs. However, considering the substantial burden of these patients, their need for adequate treatment and the substantial evidence supporting the efficacy of these treatments, advancing dissemination of treatment and empirical knowledge seems to be a worthwhile future investigation.

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References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC, USA: Author.

Arntz, A., Stupar-Rutenfrans, S., Bloo, J., van Dyck, R., & Spinhoven, P. (2015). Prediction of treatment discontinuation and recovery from Borderline Personality Disorder: Results from an RCT comparing schema therapy and transference focused psychotherapy. *Behaviour Research and Therapy, 74*, 60-71. https://doi.org/10.1016/j.brat.2015.09.002

Bales, D., van Beek, N., Smits, M., Willemsen, S., Busschbach, J. J. V., Verheul, R., & Andrea, H. (2012). Treatment outcome of 18-month, day hospital mentalization-based treatment (MBT) in patients with severe borderline personality disorder in the Netherlands. *Journal of Personality Disorders, 26*(4), 568-582. https://doi.org/10.1521/pedi.2012.26.4.568

Barnicot, K., Katsakou, C., Marougka, S., & Priebe, S. (2011). Treatment completion in psychotherapy for borderline personality disorder: A systematic review and meta-analysis. *Acta Psychiatrica Scandinavica, 123*(5), 327-338. https://doi.org/10.1111/j.1600-0447.2010.01652.x

Bateman, A., & Fonagy, P. (1999). Effectiveness of partial hospitalization in the treatment of borderline personality disorder: A randomized controlled trial. *The American Journal of Psychiatry, 156*(10), 1563-1569. https://doi.org/10.1176/ajp.156.10.1563

Bateman, A., & Fonagy, P. (2008). 8-year follow-up of patients treated for borderline personality disorder: Mentalization-based treatment versus treatment as usual. *The American Journal of Psychiatry, 165*(5), 631-638. https://doi.org/10.1176/appi.ajp.2007.07040636

Bateman, A., & Fonagy, P. (2009). Randomized controlled trial of outpatient mentalization-based treatment versus structured clinical management for borderline personality disorder. *The American Journal of Psychiatry, 166*(12), 1355-1364. https://doi.org/10.1176/appi.ajp.2009.09040539

Bateman, A., & Fonagy, P. (2016). *Mentalization-based treatment for personality disorders: A practical guide*. Oxford, United Kingdom: Oxford University Press.

Bateman, A., & Fonagy, P. (Eds.). (2019). *Handbook of mentalizing in mental health practice* (2nd ed.). Washington, DC, USA: American Psychiatric Association Publishing.

Bateman, A., O'Connell, J., Lorenzini, N., Gardner, T., & Fonagy, P. (2016). A randomised controlled trial of mentalization-based treatment versus structured clinical management for patients with comorbid borderline personality disorder and antisocial personality disorder. *BMC Psychiatry, 16*, Article 304. https://doi.org/10.1186/s12888-016-1000-9

Brazier, J. E., Tumur, I., Holmes, M., Ferriter, M., Parry, G., Dent-Brown, K., & Paisley, S. (2006). *Psychological therapies including dialectical behaviour therapy for borderline personality disorder: A systematic review and preliminary economic evaluation* (NIHR Health Technology Assessment programme: Executive Summaries). Southampton, United Kingdom.

Calati, R., & Courtet, P. (2016). Is psychotherapy effective for reducing suicide attempt and non-suicidal self-injury rates? Meta-analysis and meta-regression of literature data. *Journal of Psychiatric Research, 79*, 8-20. https://doi.org/10.1016/j.jpsychires.2016.04.003

Clarkin, J. F., Cain, N. M., & Lenzenweger, M. F. (2018). Advances in transference-focused psychotherapy derived from the study of borderline personality disorder: Clinical insights with a focus on mechanism. *Current Opinion in Psychology, 21*, 80-85. https://doi.org/10.1016/j.copsyc.2017.09.008

Clarkin, J. F., Levy, K. N., Lenzenweger, M. F., & Kernberg, O. F. (2007). Evaluating three treatments for borderline personality disorder: A multiwave study. *The American Journal of Psychiatry, 164*(6), 922-928. https://doi.org/10.1176/ajp.2007.164.6.922

Cristea, I. A., Gentili, C., Cotet, C. D., Palomba, D., Barbui, C., & Cuijpers, P. (2017). Efficacy of psychotherapies for borderline personality disorder: A systematic review and meta-analysis. *JAMA Psychiatry, 74*(4), 319-328. https://doi.org/10.1001/jamapsychiatry.2016.4287

De Meulemeester, C., Vansteelandt, K., Luyten, P., & Lowyck, B. (2018). Mentalizing as a mechanism of change in the treatment of patients with borderline personality disorder: A parallel process growth modeling approach. *Personality Disorders, 9*(1), 22-29. https://doi.org/10.1037/per0000256

Doering, S., Hörz, S., Rentrop, M., Fischer-Kern, M., Schuster, P., Benecke, C., . . . Buchheim, P. (2010). Transference-focused psychotherapy v. treatment by community psychotherapists for borderline personality disorder: Randomised controlled trial. *The British Journal of Psychiatry, 196*(5), 389-395. https://doi.org/10.1192/bjp.bp.109.070177

Fischer-Kern, M., Doering, S., Taubner, S., Hörz, S., Zimmermann, J., Rentrop, M., . . . Buchheim, A. (2015). Transference-focused psychotherapy for borderline personality disorder: Change in reflective function. *The British Journal of Psychiatry, 207*(2), 173-174. https://doi.org/10.1192/bjp.bp.113.143842

Foelsch, P., Schlüter-Müller, S., Odom, A., Arena, H., Borzutzky H. A., & Schmeck, K. (2014). *Adolescent identity treatment*. Basel, Switzerland: Springer International Publishing.

Fonagy, P., Gergely, G., Jurist, E. J., & Target, M. (2002). *Affect regulation, mentalization and the development of the self*. London, United Kingdom: Karnac Books.

Fonagy, P., Luyten, P., & Bateman, A. (2017). Treating borderline personality disorder with psychotherapy: Where do we go from here? *JAMA Psychiatry, 74*(4), 316-317. https://doi.org/10.1001/jamapsychiatry.2016.4302

Fonagy, P., Luyten, P., & Strathearn, L. (2011). Borderline personality disorder, mentalization, and the neurobiology of attachment. *Infant Mental Health Journal, 32*(1), 47-69. https://doi.org/10.1002/imhj.20283

Giesen-Bloo, J., van Dyck, R., Spinhoven, P., van Tilburg, W., Dirksen, C., van Asselt, T., . . . Arntz, A. (2006). Outpatient psychotherapy for borderline personality disorder: Randomized trial of schema-focused therapy vs transference-focused psychotherapy. *Archives of General Psychiatry, 63*(6), 649-658. https://doi.org/10.1001/archpsyc.63.6.649

Gonzalez-Torres, M. A. (2018). Psychodynamic psychotherapies for borderline personality disorders. Current developments and challenges ahead. *BJPsych International, 15*(1), 12-14. https://doi.org/10.1192/bji.2017.7

Goodman, G. (2013). Is mentalization a common process factor in transference-focused psychotherapy and dialectical behavior therapy sessions? *Journal of Psychotherapy Integration, 23*(2), 179-192. https://doi.org/10.1037/a0032354

Grant, B. F., Chou, S. P., Goldstein, R. B., Huang, B., Stinson, F. S., Saha, T. D., . . . Ruan, W. J. (2008). Prevalence, correlates, disability, and comorbidity of DSM-IV borderline personality disorder: Results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *The Journal of Clinical Psychiatry, 69*(4), 533-545. https://doi.org/10.4088/JCP.v69n0404

Gunderson, J. G., Weinberg, I., & Choi-Kain, L. (2013). Borderline personality disorder. *Focus, 11*(2), 129-145. https://doi.org/10.1176/appi.focus.11.2.129

Jobst, A., Hörz, S., Birkhofer, A., Martius, P., & Rentrop, M. (2010). Psychotherapists' attitudes towards the treatment of patients with borderline personality disorder. *Psychotherapie, Psychosomatik, Medizinische Psychologie, 60*(3/04), 126-131. https://doi.org/10.1055/s-0029-1220764

Jørgensen, C. R., Freund, C., Bøye, R., Jordet, H., Andersen, D., & Kjølbye, M. (2013). Outcome of mentalization-based and supportive psychotherapy in patients with borderline personality disorder: A randomized trial. *Acta Psychiatrica Scandinavica, 127*(4), 305-317. https://doi.org/10.1111/j.1600-0447.2012.01923.x

Juanmartí, F. B., & Lizeretti, N. P. (2017). Eficacia de la psicoterapia para el tratamiento del Trastorno Límite de la Personalidad: Una revisión. *Papeles Del Psicólogo – Psychologist Papers, 37*(1), 148-156. https://doi.org/10.23923/pap.psicol2017.2832

Kernberg, O. (1967). Borderline personality organization. *Journal of the American Psychoanalytic Association, 15*(3), 641-685. https://doi.org/10.1177/000306516701500309

Kernberg, O. F. (2016). New developments in transference focused psychotherapy. *The International Journal of Psycho-Analysis, 97*(2), 385-407. https://doi.org/10.1111/1745-8315.12289

Leichsenring, F., Leibing, E., Kruse, J., New, A. S., & Leweke, F. (2011). Borderline personality disorder. *The Lancet, 377*(9759), 74-84. https://doi.org/10.1016/S0140-6736(10)61422-5

Lemma, A., Target, M., & Fonagy, P. (2011). The development of a brief psychodynamic intervention (dynamic interpersonal therapy) and its application to depression: A pilot study. *Psychiatry, 74*(1), 41-48. https://doi.org/10.1521/psyc.2011.74.1.41

Levy, K. N., Meehan, K. B., Kelly, K. M., Reynoso, J. S., Weber, M., Clarkin, J. F., . . . Kernberg, O. F. (2006). Change in attachment patterns and reflective function in a randomized control trial of transference-focused psychotherapy for borderline personality disorder. *Journal of Consulting and Clinical Psychology, 74*, 1027-1040. https://doi.org/10.1037/0022-006X.74.6.1027

Luyten, P., Blatt, S. J., & Fonagy, P. (2013). Impairments in self structures in depression and suicide in psychodynamic and cognitive behavioral approaches: Implications for clinical practice and research. *International Journal of Cognitive Therapy, 6*(3), 265-279. https://doi.org/10.1521/ijct.2013.6.3.265

McLaughlin, S. P. B., Barkowski, S., Burlingame, G. M., Strauss, B., & Rosendahl, J. (2019). Group psychotherapy for borderline personality disorder: A meta-analysis of randomized-controlled trials. *Psychotherapy, 56*(2), 260-273. https://doi.org/10.1037/pst0000211

Milrod, B., Leon, A. C., Busch, F., Rudden, M., Schwalberg, M., Clarkin, J., . . . Shear, M. K. (2007). A randomized controlled clinical trial of psychoanalytic psychotherapy for panic disorder. *The American Journal of Psychiatry, 164*(2), 265-272. https://doi.org/10.1176/ajp.2007.164.2.265

Normandin, L., Ensink, K., Yeomans, F. E., & Kernberg, O. F. (2014). Transference-focused psychotherapy for personality disorders in adolescence. In C. Sharp & J. L. Tackett (Eds.), *Handbook of borderline personality disorder in children and adolescents* (pp. 333-359). New York, NY, USA: Springer.

Oldham, J. M. (2006). Borderline personality disorder and suicidality. *The American Journal of Psychiatry, 163*(1), 20-26. https://doi.org/10.1176/appi.ajp.163.1.20

Olesen, J., Gustavsson, A., Svensson, M., Wittchen, H.-U., & Jönsson, B. (2012). The economic cost of brain disorders in Europe. *European Journal of Neurology, 19*(1), 155-162. https://doi.org/10.1111/j.1468-1331.2011.03590.x

OPD Taskforce. (Eds.). (2008). *Operationalized Psychodynamic Diagnosis OPD-2: Manual of diagnosis and treatment planning*. Cambridge, MA, USA: Hogrefe & Huber.

Oud, M., Arntz, A., Hermens, M. L., Verhoef, R., & Kendall, T. (2018). Specialized psychotherapies for adults with borderline personality disorder: A systematic review and meta-analysis. *The Australian and New Zealand Journal of Psychiatry, 52*(10), 949-961. https://doi.org/10.1177/0004867418791257

Rossouw, T. I., & Fonagy, P. (2012). Mentalization-based treatment for self-harm in adolescents: A randomized controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry, 51*(12), 1304-1313.e3. https://doi.org/10.1016/j.jaac.2012.09.018

Salvador-Carulla, L., Bendeck, M., Ferrer, M., Andión, O., Aragonès, E., & Casas, M. (2014). Cost of borderline personality disorder in Catalonia (Spain). *European Psychiatry, 29*(8), 490-497. https://doi.org/10.1016/j.eurpsy.2014.07.001

Shedler, J. (2010). The efficacy of psychodynamic psychotherapy. *American Psychologist, 65*(2), 98-109. https://doi.org/10.1037/a0018378

Smits, M. L., Feenstra, D. J., Eeren, H. V., Bales, D. L., Laurenssen, E. M. P., Blankers, M., . . . Luyten, P. (2019). Day hospital versus intensive out-patient mentalisation-based treatment for borderline personality disorder: Multicentre randomised clinical trial. *The British Journal of Psychiatry*. Advance online publication. https://doi.org/10.1192/bjp.2019.9

Stoffers, J. M., Völlm, B. A., Rücker, G., Timmer, A., Huband, N., & Lieb, K. (2012). Psychological therapies for people with borderline personality disorder. *The Cochrane Database of Systematic Reviews,* 8, Article CD005652. https://doi.org/10.1002/14651858.CD005652.pub2

Torgersen, S. (2005). Epidemiology. In J. M. Oldham, A. E. Skodol, & D. S. Bender (Eds.), *The American Psychiatric Publishing textbook of personality disorders* (pp. 129–141). Washington, DC, USA: American Psychiatric Publishing.

Trull, T. J., Jahng, S., Tomko, R. L., Wood, P. K., & Sher, K. J. (2010). Revised NESARC personality disorder diagnoses: Gender, prevalence, and comorbidity with substance dependence disorders. *Journal of Personality Disorders, 24*(4), 412-426. https://doi.org/10.1521/pedi.2010.24.4.412

van Asselt, A. D. I., Dirksen, C. D., Arntz, A., Giesen-Bloo, J. H., van Dyck, R., Spinhoven, P., . . . Severens, J. L. (2008). Out-patient psychotherapy for borderline personality disorder: Cost-effectiveness of schema-focused therapy v. transference-focused psychotherapy. *The British Journal of Psychiatry, 192*(6), 450-457. https://doi.org/10.1192/bjp.bp.106.033597

Victorian Government Department of Human Services. (2005). *Victorian Burden of Disease Study.* Melbourne, Australia: Author.

Volkert, J., Gablonski, T.-C., & Rabung, S. (2018). Prevalence of personality disorders in the general adult population in Western countries: Systematic review and meta-analysis. *The British Journal of Psychiatry, 213*(6), 709-715. https://doi.org/10.1192/bjp.2018.202

Wagner, T., Roepke, S., Marschall, P., Stiglmayr, C., Renneberg, B., Gieb, D., . . . Fydrich, T. (2013). Krankheitskosten der Borderline Persönlichkeitsstörung aus gesellschaftlicher Perspektive. *Zeitschrift für Klinische Psychologie und Psychotherapie, 42*(4), 242-255. https://doi.org/10.1026/1616-3443/a000227

Whitehorn, J. C., Braceland, F. J., Lippard, V. W., & Malamud, W. (Eds.). (1953). *The Psychiatrist: His training and development.* Washington, DC, USA: American Psychiatric Association.

Yeomans, F. E., Clarkin, J. F., & Kernberg, O. F. (2015). *Transference-focused psychotherapy for borderline personality disorder: A clinical guide.* Washington, DC, USA: American Psychiatric Publishing.

Yeomans, F. E., Levy, K. N., & Caligor, E. (2013). Transference-focused psychotherapy. *Psychotherapy, 50*(3), 449-453. https://doi.org/10.1037/a0033417

Zerbo, E., Cohen, S., Bielska, W., & Caligor, E. (2013). Transference-focused psychotherapy in the general psychiatry residency: A useful and applicable model for residents in acute clinical settings. *Psychodynamic Psychiatry, 41*(1), 163-181. https://doi.org/10.1521/pdps.2013.41.1.163

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Competences of Clinical Psychologists

EACLIPT Task Force On "Competences of Clinical Psychologists"

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Abstract

Background: Politicians, societies, stakeholders, health care systems, patients, their relatives, their employers, and the general population need to know what they can expect from clinical psychologists. Even more, for our self-definition as a professional group, we should share a common understanding of the competence profile that characterises our qualifications. This understanding of the competence profile of clinical psychology leads directly to the content that should be taught in university curricula and postgraduate trainings for clinical psychology. The following discussion paper attempts to offer a general European framework for defining the competence profile of clinical psychologists.

Method: A group of European specialists developed this discussion paper under the umbrella of the European Association of Clinical Psychology and Psychological Treatment (EACLIPT). Representatives with different treatment orientations, of basic science and clinical applications, and from East to Western European countries, were part of the group.

Results: We present a list of competences that should be acquired during regular studies of psychology with a clinical specialisation. Additionally, further competences should be acquired either during studying, or during postgraduate trainings.

Conclusion: Clinical psychologists are experts in mental and behavioural disorders, their underlying psychological, social and neurobiological processes, corresponding assessments/diagnostic tools, and evidence-based psychological treatments. While we provide a list with all competences of clinical psychologists, we do not consider this proposal as a final list of criteria, but rather as a living discussion paper that could be updated regularly. Therefore, we invite our colleagues to contribute to this discussion, and to submit comments via email to the corresponding author.

Keywords

competences, clinical psychology, psychotherapy, mental disorders

Highlights

- People need to know what they can expect from clinical psychologists.
- We present a list of competences that clinical psychologists acquire during their training.
- This list of competences was developed by colleagues representing different treatment orientations, different European countries, and basic versus clinical scientists.
- This competence list can represent a basis for optimising education and training programmes for clinical psychologists, and for informing the public.

Competence lists are increasingly important for the self-definition of a profession, for the planning of study and training curricula, and for the public view on a professional field. Politicians, societies, stakeholders, health care systems, patients, their relatives, their employers, and the general population need to know what they can expect from clinical psychologists. For our self-definition as a professional group, we should share a common understanding of the competence profile that characterises our qualifications. This understanding of the competence profile of clinical psychology leads directly to the content that should be taught in university curricula and postgraduate training for clinical psychology. Therefore, competence lists can be considered as an interactive aspect of the progress of a profession: first, they are developed based on current understanding, reality, experiences, and concepts, but vice versa, the list of competences can be used to develop and improve existing training curricula to better focus on an optimised education of these necessary competences. This interaction is outlined in Figure 1.

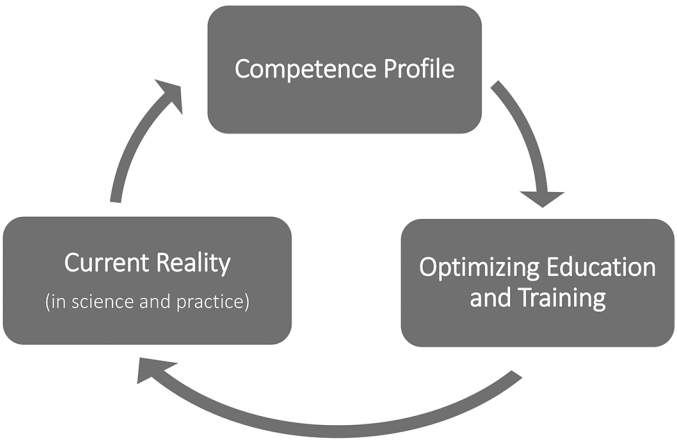

Figure 1. How competence profiles, current practice and education inform each other.

How Competence Profiles Stimulate the Progress of a Profession

Many activities exist to develop and improve competence lists for clinical psychologists and psychotherapists. However, many of them are limited to specific nations (Bartolo, 2005) or to specific psychotherapeutic orientations (Sburlati, Schniering, Lyneham, & Rapee, 2011). In the context of the IAPT programme in UK, the University College of London developed competence frameworks for specific treatment modalities and their supervision (Roth & Pilling, 2008). They also provided competence profiles for different clinical groups, and clinical contexts (ucl.ac.uk/CORE/). These kinds of competence lists serve to quality assurance, but also to ethical evaluations (Lane, 2011). Some attempts used qualitative methods to approach the field (Nodop & Strauß, 2014), and differentiated scientific-conceptual competences, personal, and interpersonal competences. Competence lists also play a role in the development of national legal regulations for psychologists and psychotherapists (Willutzki, Fydrich, & Strauß, 2015).

The aim of this article was to develop and present a European framework of competence profiles for clinical psychologists that should be valid for all evidence-based treatment orientations in all European countries. Therefore, we used the framework of the European Association of Clinical Psychology and Psychological Treatment (EACLIPT) to establish a work group representing different European countries and their national specialties, different treatment orientations, the broad range from basic to applied science, but also further aspects of diversity. The proposal was further evaluated and approved by the EACLIPT board members. Here we present the first version of the European competence list of clinical psychologists.

Competences of Clinical Psychologists

Clinical psychologists are experts in mental and behavioural disorders, the continuum from mental health to disease, psychological and psychobiological mechanisms of mental and behavioural disorders and physical diseases, epidemiological and health economic relevance of mental and behavioural disorders, vulnerability and resilience factors of psychological health, and evidence-based treatments for mental disorders and psychological factors of physical diseases. Clinical psychologists are engaged in diagnosing, treating and scientifically investigating mental and behavioural disorders and psychological factors of physical diseases within a bio-psycho-social and developmental framework. They plan, conduct, and evaluate activities to promote mental and behavioural health on a scientific basis in prevention, treatment and rehabilitation. They do not only apply current scientific knowledge, but they are also able to work with new complex problems and professional challenges, in a permanently changing environment. They have the competence

to support the scientifically-driven progress of the field, and to permanently integrate the latest scientific findings into their work.

List of Competences

More detailed competences of clinical psychologists are:

a) **General Psychological Processes in Health and Disease**
Clinical psychologists are experts in identifying and describing psychological, psychosocial, psychobiological and neuroscientific aspects of normal and abnormal human behaviour and experiences, hereby considering the whole life span. They have expertise in analysing the role of cognitive processes such as perception, learning, memory, language, of emotional and motivational processes, in developmental psychology and developmental psychopathology of the whole life span, of the biological basis of human experiences and behaviour, individual differences and dimensions of personality, and they can identify the social and cultural influences on normal and abnormal behaviour and experiences. They are familiar with scientifically sound models to better understand normal and abnormal behaviour, and can apply them to understand and treat psychological problems across life span.

b) **Mental and Behavioural Disorders and Psychological Processes in Physical Disorders**
Clinical psychologists are experts in informing the public, political stakeholders, institutions, affected people and their relatives about psychological problems and mental disorders, their varying appearances, and how to classify them. They can also identify psychological and psychosocial aspects of physical diseases. They are able to detect, diagnose, classify and describe mental disorders and psychological processes of physical diseases, using observational techniques, self-rating scales, expert ratings and other evaluated assessment tools. Clinical psychologists reflect on cultural, societal and historical relativism in diagnosing mental and behavioural disorders and continually contribute to the development of international classification systems.

c) **Psychological Diagnostics**
Clinical psychologists are able to develop, evaluate, employ, analyse, and report results of diagnostic tools to improve the objectivity, reliability and validity of diagnosing psychological, psychosocial and neurobiological aspects of mental and behavioural disorders and psychological mechanisms relevant in physical diseases. In their diagnostic work, they consider the continuum between healthy and clinically relevant processes, age- and socioeconomically relevant aspects, and other environmental and cultural determinants of psychological well-being and dysfunctional processes. They employ best-evidence self-rating scales, scientifically evaluated interview techniques, and other assessment tools, both for clinical

purposes, but also to assess personality characteristics, performance profiles, deficits, skills, and resources.

d) Intervention: General Aspects

Clinical psychologists know about the different evidence-based psychological interventions, their historical development and current evidence-based evaluation. They can critically think about different treatments and can inform the public about scientifically based treatment guidelines and typical treatment characteristics, hereby considering disorder-, person- and sociocultural-relevant aspect. They use scientifically-based interventions to enhance resources of the patients and clients to improve psychological well-being, and to reduce vulnerability and risk factors for psychological problems and mental and behavioural disorders. Clinical psychologists can inform patients, their relatives, public institutions, stakeholders and others about the potential and risks of psychological treatments, based on a current critical scientific evaluation of them.

e) Prevention, Rehabilitation: General Academic Expertise

Clinical psychologists are able to inform about prevention and rehabilitation programmes, their scientific evidence, and their potential use for society and specific target groups. They can develop, apply and evaluate such programmes. Clinical psychologists can promote mental and behavioural health and develop mental health literacy in various settings.

f) Scientific Methodology

Clinical psychologists can use qualitative and quantitative approaches to investigate psychological, psychobiological and psychosocial processes and clinical applications to better understand normal and abnormal behaviour and experiences. They are able to plan, conduct and analyse the results of studies using modern criteria for scientific evaluations and advanced statistical modelling. In particular, clinical psychologists are able to plan, conduct, analyse, report and explain clinical trials and their results, to evaluate psychological interventions according to modern scientific standards. They are also able to understand and use methods and results from developmental, cognitive and experimental psychology, or from any other field related to scientific psychology important for the understanding of the aetiology, maintenance and treatment of mental and behavioural disorders. They know methods and central elements of psychotherapy and psychological intervention research, and how to incorporate that knowledge into their clinical practice. They actively take part in psychological intervention and psychotherapy research by developing research questions, designs and treating patients in clinical trials.

g) Ethical and Legal Aspects

Clinical psychologists consider and respect current ethical standards and legal regulations for their professional work. Clinical psychologists are sensible regarding cultural diversity and respect it in their work with clients.

Depending on national regulations, the following skills are either acquired during university studies, or during postgraduate trainings often connected to the term psychotherapy:

h) Skills for Psychological Interventions: Meta-Competences

- Clinical psychologists are able to provide psychological interventions that follow treatment aims and a treatment plan, based on current scientific knowledge about mental and behavioural disorders and interventions. Major competences to provide interventions have been acquired according to current standards of learning how to practise these interventions.
- Clinical psychologists are able to motivate patients to engage in psychological interventions, and to foster and maintain a good alliance with their clients/patients, their relatives and significant others. They can explain the intervention rationale to patients, other health care specialists, and further involved people.
- Clinical psychologists have the competence for perspective taking, empathy and mentalisation. They have professional skills to identify the diversity of verbal and nonverbal communication signals of others. They have professional competences to communicate with others, based on a broad variety of acquired communication skills, even during difficult communication sequences, or with patients with difficult communication patterns. They can verbally address emotional, cognitive, behavioural and interactive aspects of the patient's/client's behaviour.
- Clinical psychologists have an advanced ability to regulate their own emotions and behaviour, and to reflect their own emotions, cognitions, and behaviour during professional encounters. They can reflect the consequences of past learning and socialisation processes on current behaviour and experiences, not only in others, but also in themselves. They can cope with professional stressful situations, but are able to relax and plan their life according to an adequate work-life-balance.
- Clinical psychologists are able to evaluate on-going interventions of themselves or of others, to detect unfavourable or unexpected events, and to react adequately in the event of occurring risks (e.g., suicidality). They are able to address treatment problems (e.g. adherence problems of patients) and problems of the therapeutic relationship accordingly. They are able to use the patient's/client's feedback to adapt intervention processes.
- When confronted with new problematic professional situations, they have concepts about how to develop new problem-solving strategies, based on a profound framework theory how to plan interventions.
- Clinical psychologists are able to end interventions in a planned manner, to plan for long-term maintenance of treatment gains, and to reduce the risk of relapse after the intervention.

- Clinical psychologists aim to continuously improve their professional abilities. They are able to learn from their own and other experiences, from supervision and intervision, and to transfer current scientific knowledge to clinical practice and to integrate recommendations of others (e.g. supervisors) in their clinical work.
- Clinical psychologists are able to communicate with other health-professionals, and to coordinate their diagnostic and intervention plans with other experts involved in the overall treatment plan.

i) **Skills for Psychological Interventions: Disorder-, Person-, and Context-Specific Diagnostics and Interventions**
Following recommendations of official scientifically based guidelines, clinical psychologists can select evidence-based diagnostic tools and evidence-based psychological interventions for specific mental and behavioural disorders and psychological aspects of physical diseases. For treatment planning, they consider the different severity degrees and courses of mental and behavioural disorders, the comorbidity profiles, further associated problems, the patient's and setting's resources, as well as cultural aspects.

j) **Skills for Psychological Interventions: Prevention, Rehabilitation**
Clinical psychologists are able to prepare, conduct, and evaluate clinical prevention and rehabilitation programmes according to current scientific standards. They have public relation skills to present programmes and persuasive skills to promote the relevance of the programmes to significant stakeholders.

k) **Skills for Psychological Interventions: Setting-Specific Interventions, Modern Technologies**
Clinical psychologists are able to provide professional, scientifically based work with individuals, with couples, with families, and in groups. They can provide expert knowledge and they have the ability to work in complex systems (e.g., hospitals, occupational health services, political institutions). They are aware of options to increase effectivity, reachability, and benefit-cost-ratios for providing clinical psychological interventions also by using modern technologies.

l) **Skills for Psychological Interventions: Documentation, Evaluation**
Clinical psychologists continuously document and evaluate their work. They consider aspects of quality insurance.

Conclusion

We provide a first list with the characterising competences of clinical psychologists that aims to cover the needs of all European nations, but also of representatives of different specialisations and orientations of clinical psychology. However, we do not consider this proposal as an exhaustive list of criteria, but as a living discussion paper that could be

updated regularly. Therefore, we invite our colleagues to contribute to this discussion, and to submit comments via email to the corresponding author.

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References

Bartolo, P. A. (2005). Regulating the psychology profession in Malta. *European Psychologist, 10*(1), 76-77. https://doi.org/10.1027/1016-9040.10.1.76

Lane, D. (2011). Ethics and professional standards in supervision. In T. Bachkirova, P. Jackson, & D. Clutternuck (Eds.), *Coaching and mentoring supervision: Theory and practice* (pp. 99–104). Maidenhead, United Kingdom: Open University Press.

Nodop, S., & Strauß, B. (2014). Kompetenzbereiche in der psychotherapeutischen Ausbildung. *Zeitschrift für Klinische Psychologie und Psychotherapie, 43*(3), 171-179. https://doi.org/10.1026/1616-3443/a000272

Roth, A. D., & Pilling, S. (2008). *A competence framework for the supervision of psychological therapies*. Retrieved August, 18, 2011 from www.ucl.ac.uk/CORE/.

Sburlati, E. S., Schniering, C. A., Lyneham, H. J., & Rapee, R. M. (2011). A model of therapist competencies for the empirically supported cognitive behavioral treatment of child and adolescent anxiety and depressive disorders. *Clinical Child and Family Psychology Review, 14*(1), 89-109. https://doi.org/10.1007/s10567-011-0083-6

Willutzki, U., Fydrich, T., & Strauß, B. (2015). Aktuelle Entwicklungen in der Psychotherapieausbildung und der Ausbildungsforschung. *Psychotherapeut, 60*(5), 353-364. https://doi.org/10.1007/s00278-015-0048-1

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