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Chapter 6

THE EFFECTS OF PHARMACOTHERAPY IN PSYCHIATRY: IMPACT, PERCEPTION AND INTERPRETATION

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ABSTRACT

Biological activity of psychopharmacological agents extends from intracellular level to its impact on highly integrated mental functions. On this last mentioned level, pharmacological agents modulate salience (antipsychotics) and emotional processing, processing of social cues, emotional memory, attentional vigilance, and threat processing (antidepressants and anxiolytics). This level of the effect of medication is situated at the border of person's abilities to perceive it and then verbalize it. The effect of medication is then subjectively perceived in the context of individual insight and personality (on the basis of emotional, cognitive, behavioural or social context). The perceptions of the effects of medication are then interpreted by patient, physician and all other persons directly or indirectly involved in psychopharmacological process. The ultimate description and evaluation of pharmacology is based on this last process of interpretation.

Keywords: pharmacotherapy, psychiatry, perception, interpretation, psychosis, anxiety, depression

INTRODUCTION

It is the aim of this paper to present the observations made in the course of clinical work, against the background of recent scientific publications on the impact of medication in the

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pharmacotherapy of mental diseases and disorders. Based on these two sources (clinical observation and analysis of the literature) an attempt has been made here to form certain generalizations, and draw conclusions from a range of basic phenomena taking place in the course of pharmacological treatment in psychiatry.

The effects of medication are perceptible on many levels; starting with sub-cellular levels, the effects that drugs have on the activity of receptors and neurotransmitters, following to more complex neurological brain systems, and finally to the modification of the perception of essential stimuli and representations, including the ways information is processed in the brain. None of these stages are available to direct subjective perception; no one is directly aware of them and they cannot be verbalised. In fact, the effects of medication are verbalized after a subjective perception of their impact. The perception of the activity of medication takes place on a level different to where it actually happens, yet it is accessible to consciousness. For example, let us assume that antidepressants have an impact on processing emotional information. Our subjective perceptions will not be about this level of their activity, instead, they will focus on the indirect effects of medication, which might be verbalized as “I cry less” or “I go out more”. Individually observed effects of medication are a far-transformed and based on individual factors way of transcribing the real impact of medication into subjectively perceived changes, and ways of verbalising them, whereas the subjectively perceived impact of medication and the related change in patient’s behaviour provide a basis for interpreting the impact of medication and the effects of treatment. These interpretations are made by everyone involved in the treatment process directly or indirectly. They are of individual character and are a combination of individual contexts of all these people, and therefore might be, and often are, mutually contradictory. It is, however, only the interpretation level that gives a final shape to the effects of treatment and makes its evaluation possible.

Perceptions of the clinical effects of medication in a medical context i.e. as “improved mood”, “disappearance of psychotic symptoms” are processes very far from the real activity of medication, based on the complex cognitive concepts (e.g. depression, psychosis) that are encoded through education in a doctor’s mind, but they are nevertheless useful.

And so the processes that take place between the time medication is administered, taken and the effects of its activity are observed, are rarely noticed as they happen on many levels. The aim of this paper is therefore to propose three separate stages, each of them with a very complex inner structure and practically unlimited number of variations. These stages are:

- basic biological activity of medication on many levels of brain/mind functions
- perceptions of this biological activity
- interpretation of the biological impact by many people involved in therapy and in a variety of contexts.

Each of the stages proposed here, involves a great deal of phenomena, taking place on many levels and in many contexts. It is enough to realize how much information we actually have on the biological activity of medication, starting with sub-cellular and cellular level, all the way to its impact on information processing, and the level of its activity affecting psychopathological symptoms in the course of pharmacologically treated illnesses.

The presentation of such knowledge would require a multifaceted approach, in which the principal concept of this paper would be lost. This is why it is important to be aware of the fact that each of the stages of pharmacotherapy sketched here has practically infinite number of variations and is influenced by multiple factors, yet listing them all is not a subject of this work. The main reason for leaving out excessive detail is opting out for clear presentation the main concept. So going back to the example quoted before, the possible number of genetic, metabolic, individual pharmacokinetic, possible interactions, and other variables that have an impact on the pharmacological workings of medication is difficult to evaluate and practically almost impossible to describe. So for the clarity of argument, I suggest accepting the premise that medication causes biological activity, although in other contexts it is important to realize that this is not the case in all circumstances and that the impact we are talking about here might be extremely individually varied. Similarly, it is impossible within one paper do discuss all the factors that influence the stage of perceiving the activity of medication. This is because the number of factors influencing the interpretation of the activity of medication, the number of contexts in which interpretations are made and their changeability throughout time leave us with two options: choosing casuistic descriptions and making high level generalizations that summarise the discussed phenomena or grouping them into very spacious categories.

BIOLOGICAL ACTIVITY OF MEDICATION

Biological activity of drugs takes place on many levels, beginning with sub-cellular structures, through the level of synapses and receptors, activities of neuronal systems (dopaminergic, serotonergic etc.), neuroplasticity, lipid peroxidation and finally more complex brain systems and probably in many other dimensions. The activity of medication within the biological systems mentioned here is not accessible to direct subjective observation.

It is expressed on the level of more integrated brain/mind functions, which lie beyond the boundary open to direct perception and verbalization based on subjective experience. For example antipsychotic drugs dampen excessive salience of external stimuli and internal representations [1, 2, 3]. In this case the mesolimbic dopamine system that is overactive in psychosis is calmed down, which stops the psychotic process of attributing aberrant salience to otherwise neutral external stimuli. In effect, a persons treated with antipsychotic drugs experiences lower intensity of signals and representations identified as “meaningful”, and clinically they no longer refer all external signals originating in their environment to themselves. Similar processes can be detected in the treatment of depression. As many recent research results indicate [4, 5, 6, 7, 8, 9], the impact of antidepressants may change the ways in which emotionally relevant information or social stimuli are being processed. It also dulls the sensitivity to information in interactions with other people and affects emotional memory. Depressive persons display certain characteristic bias in processing emotionally charged information and interactions, and the research quoted above also implies that the effects of antidepressants can modify the distorted reception of signals and information analysis. Also new studies are being published that discuss the way in which anxiolytics (diazepam) modify

perception centres, processing information of a social character or stimuli that cause anxiety. [10] Yet still these changes are still impossible to be perceived and named directly.

A helpful analogy may be found in the impact of antibiotics on bacteria that respond to it – the process is also outside of the reach of subjective perception. What can be perceived, however, at the beginning of the treatment is general impressions, such as “I feel somehow better”, and then specific manifestations of clinical improvement, such as “lowering body temperature, or intensity of other symptoms, such as cough, muscle pains etc.”

Psychoactive drugs can be discussed in the analogical context. Their impact on both sub-cellular and receptor level, and the level of integrated neuronal systems is not subjectively perceived. The way this medication works at the higher levels of the organisation of neurological systems can not be perceived subjectively (patients never mention the “improvement in processing emotional information” as the description of what is happening to them or “the reduction in attributing excessive salience to external stimuli”).

Future research will certainly provide new data about the way medication used in psychiatry essentially works, especially with respect of more integrated brain/mind functions. They will certainly focus on the complex impact of medication on processing information in the brain, its influence on the analysis of information perceived from the outside, attention, memory and other functions. However, it seems that the principle described in this paper may still be treated as universal. The biological activity of medication on many levels remains impossible to perceive subjectively. On more complex levels, however, such as for example information processing, it lies on the boundary between unclear subjective perception originating at a biological level and the possibility to perceive things consciously. It is clear though that the clinical effects of medication must be perceived and noticed in the context of an individual person, and it is only as a result of this subjective perception that the information that “the drug works” emerges in the awareness of the treated person.

PERCEPTION OF THE IMPACT OF MEDICATION

The effect of the activity of medication must be subjectively perceived by a patient, doctor or other people, such as the patient’s family, other patients, nurses, ward managers etc. This perception does not take place, however, on the level that the drug „actually” works at i.e. on the level described above. It is rather focused on the subjective perception of change in perceiving things, thinking, emotional responses, behaviour, relations with other people etc.

This perception can vary in character, for example it can be:

- sensory (“I have begun to notice colours”)
- somatic (“I’m not in so much pain now”)
- cognitive (“My thoughts are clearer”)
- emotional (“I can feel my emotions again”)
- observation of behaviour (“I cry less and smile more”)
- mood changes (“My mood has improved”)
- physical fitness (“I can walk faster”)
- increased level of activity (“I began going out again”)
- social relations (“I’m in touch with people again”)

And so a patient who is treated with an antipsychotic drug can, for example, notice that she is no longer stared at in the street. A patient with depression can notice that she cries less or that she can see colours more vividly. She will not notice how the drug actually affects her subjective experience but the perception will be indirect in character; a patient will simply notice certain subjective displays of the impact of medication.

In the first stages of the activity of medication, the process itself takes place on the border between a biological and subjective level, which means that the effects of its activity, such as changes in the way one feels might be subjectively felt on a psychosomatic level (feelings, impressions, sensations of unspecific general change), but they can not be fully verbalized on the conscious level. In schizophrenia, this is reflected in the research on the early subjective response to neuroleptics. [11]. The response, tested 24 and 48 hours after the first dosage of medication is taken, is based on subjectively felt biological changes caused by medication. What's important and interesting is that it allows for forecasting the efficiency of treatment over a period of a few weeks (early positive response correlates with positive clinical response to administered medication.) In this and the next stages of the activity of medication, a process takes place which has an additional effect on the dimensions described above – the process referred to as a “placebo effect”. Kapsambelis has noted that “... the notion of placebo effect is somehow inaccurately used when it comes to psychoactive drugs.” [12]

It is because the problem that appears in psychiatry is that the impact area of psychoactive drugs is identical to the area where the effect of the influence of one mind on another takes place, one psyche on another.” [12, p.123]. In biological dimensions the “placebo” and “nocebo” effects are accompanied by a corresponding increase or decrease of endogenous dopamine transmission and excretion of opioids. [13]

And so both of these effects have simultaneously a psychological (expectations of the impact of medication) and biological (through the activity of appropriate neuronal systems linked to controlling the way one feels) components. The impact of medication in this context can be identified as the combined biological activity of the medication and the psychological/biological impact of the placebo or nocebo effect.

In some cases a patient might not notice the effect of the medication even if the effect is clearly perceived by other people. Sometimes a doctor or patient's family notice the changes in patient's behaviour brought about by the treatment, whereas the patient neither notices it or talks about it. This might happen for various reasons, such as the patient's intellectual deficits, lack of insights into their own emotional states, the activity of medication being different to the patient's expectations or the unconscious rejection of noticing the impact of medication due to intrapsychic conflicts.

INTERPRETATION OF THE ACTIVITY OF MEDICATION

The stage described above involves noticing certain specific manifestations of how the medication is actually working for a patient. In the next stage, these very manifestations are being interpreted by:

- the person under the treatment
- the doctor

- other professionals in the treatment context (nurses, psychologists, other doctors)
- persons close to the patient (family)
- other people in the patient's social network (acquaintances, colleagues)
- bosses, directors, insurers and other institutions involved in the process of controlling the treatment etc.

The main problem with describing this phase of treatment is linked to the fact that there might be as many of these individual interpretations as there are individual treatment processes. The interpretations can take place in very different contexts (occurring simultaneously in the same person). The interpretations of the changes observed in the patients are made by the patient, the doctor in charge, and the patient's family. Each of these people might notice different changes and interpret them differently. The contexts of these interpretations are fully individual.

For example, increased activity of a schizophrenic patient might be interpreted by the patient as a sign that the previously administered medication was harmful, and therefore it is best to stop treatment; a doctor in charge may think in terms of reduced intensity of negative symptoms, and the patient's family might feel endangered and fear that the patient's aggressive behaviour that occurred in the past might return on this occasion. Each one of the people involved in this treatment process interprets, and therefore evaluates the change that they observe differently, and this is why their treatment-related behaviour might be entirely different. These interpretations will also change throughout time. For example if a patient's increased level of activity results in his or her increased involvement in housework or employment, the family might be willing to change their interpretation of the same treatment-related processes. Because of the complexity of this stage of treatment, it is often described on two levels: first on the casuistic level and second on grouping certain phenomena related to the individual interpretations of treatment. Casuistic descriptions provide examples of very individual situations which may take place during pharmacological treatment, whereas other illustrative work provides summaries of what is going on, taking into the account various groups of phenomena that influence the interpretation of the treatment process, linked with, for example, psychopathological symptoms, levels of insight, characteristics of medication, adverse reactions to treatment etc.

Interpretation of the Effects of Medication in the Context of Diagnosing Illnesses and Dysfunctions

It is worth noting here that a doctor in charge of treatment interprets and evaluates these processes on the basis of a certain system of reference points.

- first of all, the doctors extract from the patient's account the information that they consider important in the overall context of treatment, most frequently in the context of psychopathological symptoms (for example they will consider it relevant if the patient says what she or he is in a better mood, but not if the patient has a stronger sense of smell)

- secondly the doctor makes use of very complex conceptual notions, such as depressive disorder, positive symptoms, negative symptoms, psychosis.

Therefore, it appears there is a very complex correlation in many intermediate stages between the “real” activity of medication and the doctor noticing it on a clinical level, in relation how the psychopathological symptoms are disappearing or to the treatment of a specific illness. This “real” activity of medication may include, for example, its impact on distorted processing of information, whereas the clinical evaluation is formulated on the level of the overall improvement in a certain group of symptoms distinguished “apriori” or based on the fact that “the episode of the illness is disappearing”. Between these effects of medication and their interpretations on a clinical level there is a large space for the phenomena that are actually taking place and the concepts used for describing them, whose existence usually goes unnoticed.

Relevance of Doctor Patient Relationship

The doctor –patient relationship has an important impact on the phenomena presented here, at each of the stages I have attempted to identify so far. Even before a pharmacological treatment is actually undertaken, the person that comes for treatment has certain expectations and ideas about the doctor and the medication that they will be exposed to. These preconceptions are then reflected in the workings of the placebo and nocebo effect. In reference to the pharmacological impact of medication, the impact of the patient-doctor relationship on the effects of medication used in psychiatry has been described on more than one occasion. Various factors linked with this relationship such as emotional aspects, conscious and unconscious elements of the dyad (transference and countertransference) may seriously modify and sometimes even block the effects of the biological activity of medication. [14, 15, 16] Psychiatrists are often the key persons at the stage of making observations about how medication works. Based on the patient’s account, they often select the one change, that is actually the result of medication and communicate this to the patient. The doctors also communicate what is a desirable (good) effect of the medication and what is “bad” or undesirable. In this way, they essentially or sometimes even exclusively influence the subjective perceptions of the effects of the activity of medication. A similar role is played by the patient-doctor relationship at the stage of interpreting the changes in the way a patient feels and behaves. Psychiatrists provide their own interpretations and communicate them to the patient directly or indirectly by their behaviour or emotional responses to the patient), thus essentially influencing the patient’s evaluation of the observed effects of medication, their behaviour and compliance.

CONCLUSION

This paper makes an attempt to justify the thesis that there are many levels at which the biological activity of medication used in psychiatry cannot be perceived subjectively. Their impact on the integrated mental functions (for example processing of social and emotional

information, memory and attention) take place in the border areas of the possibilities of subjective perceptions, whereas the effect of the activity of medication remains observed by the patients in the context of their individual capacity for insight, mood changes in the context of personality changes. Later on, this effect is subjectively interpreted in many contexts, which gives a final shape to the evaluation of the impact of the medication used.

REFERENCES

- [1] Kapur S. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am. J. Psychiatry*. 2003 Jan;160(1):13-23.
- [2] Kapur S.: How antipsychotic become anti-psychotic – from dopamine to salience to psychosis. *Trends Pharmacol. Sc*, 2004; 25: 402-406.
- [3] Kapur S., Mizrahi R., Li M.: From dopamine to salience to psychosis –linking biology, pharmacology and phenomenology of psychosis. *Schizophr. Res.*, 2005; 79: 59-68. 16.
- [4] Harmer C.J., Bhagwagar Z., Perrett D.I., Völlm B.A., Cowen P.J., Goodwin G.M.: Acute SSRI administration affects the processing of social cues in healthy volunteers. *Neuropsychopharmacol.*, 2003; 28: 148-152.
- [5] Bowins B.: How psychiatric treatments can enhance psychological defense mechanisms. *Am. J. Psychoanalysis*, 2006;66,2, DOI: 10.1007/s11231-006-9014-6.
- [6] Harmer C.J.: Serotonin and emotional processing: does it help explain antidepressant drug action? *Neuropharmacology*, 2008; 55:1023-1028.
- [7] Harmer CJ, O'Sullivan U, Favaron E, Massey-Chase R, Ayres R, Reinecke A, Goodwin GM, Cowen PJ.: Effect of acute antidepressant administration on negative affective bias in depressed patients. *Am. J. Psychiatry*. 2009 Oct;166(10):1178-84.
- [8] Arnone D., Horder J., Cowen P.J., Harmer C.J.: Early effects of mirtazapine on emotional processing. *Psychopharmacol.*, 2009; 203: 685-691.
- [9] Tang TZ, DeRubeis RJ, Hollon SD, Amsterdam J, Shelton R, Schalet B.: Personality change during depression treatment: a placebo-controlled trial. *Arch. Gen. Psychiatry*. 2009 Dec;66(12):1322-30.
- [10] Murphy S.E., Downham C., Cowen P.J., Harmer C.J.: Direct effect of diazepam on emotional processing in healthy volunteers. *Psychopharmacol.*, 2008; 199: 503-513.
- [11] Awad A.G.: Subjective response to neuroleptics in schizophrenia. *Schizophr. Bull*. 1993;19: 609-617.
- [12] Kapsambelis V.: Pacjent, przepisujący receptę i psychosomatyczne doświadczenie leku. podejście psychoanalityczne. W: Murawiec S., Żechowski C. (red.): *Od neurobiologii do psychoterapii. Instytut Psychiatrii i Neurologii*, Warszawa 2009. s.122-139.
- [13] Scott D., Stohler C.S., Egnatuk C.M., wang H., Koeppe R.A., Zubieta J.K.: Placebo and nocebo effects are defined by opposite opioid and dopaminergic responses. *Arch. Gen. Psychiatry* 2008; 65(2): 220-231.
- [14] Murawiec S.: Psychodynamiczna interpretacja działania leków psychotropowych. W: Murawiec S., Żechowski C. (red.): *Od neurobiologii do psychoterapii. Instytut Psychiatrii i Neurologii*, Warszawa 2009. s.140-219.

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- [15] Mintz D.: Meaning and medication in the care of treatment-resistant patients. *Am. J. Psychotherapy* 2002;56: 322-335.
- [16] Mintz D., Belnap B.: A view from Riggs. Treatment resistance and patient authority – III. What is psychodynamic psychopharmacology? An approach to pharmacologic treatment resistance. *J. Am. Acad. Psychoanal. Dyn. Psychiatr.* 2006; 34: 581- 600.