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Doctor/patient relationship: the neglected power of placebo-nocebo effect

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Background

In the early '50s, the pioneering work of Michael Balint focused on the doctor-patient relationship as a critical modulating factor in the process of healing. Specifically, his aim was to transform uncertainty and difficulty in the doctor-patient relationship into a greater understanding and meaning that nurtures a more therapeutic alliance between clinician and patient. Further research indicate that the quality of doctor-patient relationship is central in:

- establishing a trusting relationship, a secure basis where a solid therapeutic alliance can be built-up and maintained;
- predicting compliance, adherence and consistence of use of different therapeutic regimens;
- enhancing hope as a powerful modulator of the healing process, the physician therefore working as a positive drug him/herself.

Two key words are central in this reading: **placebo** and **nocebo**. Placebo, future of the Latin verb *placeo*, means "I will please you, I'll do you well", thus indicating the pro-healing effects of positive expectations, that can certainly be up-regulated by a positive doctor patient-relationship. Opposite to that, nocebo, future of the Latin verb *noceo*, means "I will harm you" (involuntarily or intentionally), encompassing all the damaging effects of negative expectations. The latter can be triggered by a negative doctor-patient relationship, when distrust, neglect, negative verbal and non-verbal language, and/or aggressive behavior trigger anxiety, fear, anguish, panic, concerns, thus impairing or killing the hope of healing. However, the first understanding of this process was mainly psychological. Only recently the underlying psychobiological process has began to undergo neurobiological and instrumental scrutiny.

Aim of the presentation

To focus on the new reading of the *placebo* and *nocebo* effects in the doctor-patient relationship.

Method

Review of the literature and clinical re-thinking.

Results

Recent data from brain imaging studies indicate that the **placebo effect**

- **increases:**
 1. the **dopaminergic** pathway, thus increasing the sense of well-being, assertiveness and trust in the future, sense of empowerment and positive interactions with others;

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2. the **serotonergic** pathway, this increasing mood;
 3. the **opiate** pathway, with higher endogenous analgesia and sense of well being, joy and satisfaction, involving the same brain areas involved in the **reward system and motivated behavior**;
- and **decreases** the **adrenergic** pathway, thus reducing anxiety and fear and the overall activity of the sympathetic system.

Key areas involved are the anterior cingulate gyrus, the prefrontal cortex, the gray periaqueductal substance.

At the opposite end of the relationship spectrum, the **nocebo effect** causes **decrease of the dopaminergic, serotonergic and opiate pathways**, while increasing the corticotropin releasing pathway. This negative neurobiological effect will clinically translate into increasing anxiety and depression, that potentiate pain perception, sleep disruption, increase of fatigue and restlessness. The presentation will discuss the neurobiological correlates of placebo and nocebo effects and their clinical implications in the doctor-patient relationship.

Conclusion

Increasing evidence suggests that placebo and nocebo effect have powerful neurobiological correlates that may modulate the illness behavior and healing process. Physicians should increase their awareness on this effects, control the nocebo effect through a constant self-monitoring, and master with a higher competence the extraordinary healing potential implicit in a more human, understanding and caring doctor-patient relationship.