

## Are There Really 3 Generations of Antipsychotics?

by Norm Keltner

In October, 2002 a new antipsychotic was released to the U.S. market. Aripiprazole (Abilify) was originally touted as so new that it was presented as a third-generation medication for the people suffering from schizophrenia and other psychoses. In fact, if you were a frequent reader of ISPN's official journal in those days (i.e. Perspectives in Psychiatric Care), you may have read my 2002 article entitled, *Aripiprazole: A Third Generation of Antipsychotics Begins?* And, as some of you may remember, I had an undergraduate textbook with the inventive title, *Psychiatric Nursing*. In the 5<sup>th</sup> edition I denote aripiprazole as a third-generation drug but by the 6<sup>th</sup> edition I had placed aripiprazole with the second-generation antipsychotics.

Part of my rejection of aripiprazole as a distinctive class was simply based on these three observations: 1) Do undergraduates really care? 2) Not all authors embraced the designation of "third-generation.", and perhaps most importantly to me, 3) Can you really have a new generation of drugs if there is only one drug year after year?

That view held sway for two editions. But, as Scripture says, "...a dog returneth to his vomit" and I returned to my initial view in the 8<sup>th</sup> edition (in progress) in which I again designate aripiprazole as a third-generation antipsychotic. Perhaps the biggest contributor to my turnaround in posture has to do with objection #3- there is now more than one drug in this "generation".

In 2015, two more medications were added to the third-generation grouping. Now what is this mechanism of action that demands a third categorization? Simply, it is the fact that these three drugs do more than block D<sub>2</sub> receptors, they are partial agonists at this same receptor. Aripiprazole alone held this distinction for 14 years but no longer. Brexpiprazole (Rexulti) and cariprazine (Vraylar) are now members of that club.

Of course, new effective antipsychotics are always welcomed however one cannot help but notice that Abilify, the brand name of aripiprazole, was the #1 selling prescribed drug (meaning dollar-sales) in the U.S. during 2014-the last year it was under patent protection. Please note, it was not the #1 antipsychotic nor the #1 psychotropic drug sold. It was the #1 drug in dollar-sales period! The only other antipsychotic, in dollar-sales, in the top 100 was Seroquel at #96. It is further worth noting that brexpiprazole, one of the new drugs, is manufactured by the same company that makes Abilify and will be under patent protection for many years to come.

So, in conclusion, I believe there really are three categories of antipsychotics because 1) undergraduate students and all nurses will need to understand these highly used meds, 2) most, if not all, writers embrace the three generation concept, and 3) there is more than one drug in this category now. And to these three observations, I add a fourth observation: 4) to modify D<sub>2</sub> receptor activity with a partial agonist is distinct and important!