Recent trends in Neurophysiology research

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The biochemical exploration in man is limited by ethical and technical factors. Results are contradictory and it is only by the mean of the antidepressants used as pharmacological tools that monoaminergic hypotheses have been made. The specificity of action of these drugs is very different from one substance to another and the post synaptic impact of the antidepressants is more important than it was thought before. Finally, the monoaminergic hypothesis is too simple and cannot summarize the biochemical factors in depression.

The tricyclic and related antidepressants reduce monoamine uptake at the synapses, block the presynaptic receptors and, after chronic administration, act upon the synthesis of the monoamines and the sensitivity of the post-synaptic receptors. The NA and 5-HT synapses are influenced to different degrees by the antidepressants: for example, desipramine has a preponderance of activity at NA synapses and clomipramine at 5-HT synapses. By combining these findings and by highlighting one or other of these properties, it is possible to come to diametrically opposite conclusions upon the effect of the antidepressants upon monoamine performance (activation or inhibition) and to develop many models of the mechanisms of antidepressant action.

The recent discovery of atypical antidepressants like iprindole and mianserine which are devoid of any significant inhibitory effect on monoamine oxidase (MAOI) or on monoamine reuptake indicates that the antidepressant action is not necessarily associated with these two pharmacological effects. Systematic studies on the interactions of various antidepressants with the receptors for neurotransmitters reveal that the therapeutic action of these drugs is not related to the possible blockade of muscarinic, histaminergic, serotoninergic and/or alpha-adrenergic receptors in the CNS. However, chronic treatments with antidepressants (MAOIs, uptake inhibitors or atypical antidepressants) regularly induce a significant reduction in the number of beta-adrenergic and serotoninergic receptors in brain (particularly in the cerebral cortex of rats). This down regulation is associated with an hyposensitivity to NE and 5-HT agonists. These data further support the “monoamine theory” of depression: since down regulation is generally due to a long lasting overstimulation of receptors, it can be proposed that antidepressants increase NE and 5-HT neurotransmission in the CNS, notably in some depressed patients.

Antagonism of monoamine transport is the primary cellular action associated with many antidepressant medications. However, an increased synaptic concentration of monoamines is not the actual mechanism of antidepressant effects as suggested by the time lapse between treatment initiation and the onset of clinical antidepressant response. Chronic administration of all antidepressants increases the efficiency of 5-HT transmission in the synapse, albeit by different mechanisms. Serotonin transporter antagonists enhance serotonergic neurotransmission by decreasing the functional activity of the 5-HT1A and 5-HT1B autoreceptors. Tricyclic antidepressants and electroconvulsive therapy enhance 5-HT neurotransmission by increasing the responsiveness of postsynaptic 5-HT receptors. Monoamine oxidase inhibitors and the 5-HT1A agonists increase serotonergic function by desensitizing the somatodendritic autoreceptor; the terminal 5-HT autoreceptor is not affected by these agents. Evidence for both enhanced and diminished noradrenergic transmission following antidepressant treatment exists, although the evidence more strongly supports decreased noradrenergic transmission. Ongoing investigations into intracellular adaptations (e.g., steroid receptors, growth factors, etc.) during chronic antidepressant administration offer the promise of furthering our understanding of the mechanism of action of antidepressant

The hidden complexities of the brain are being explored by scientists working across boundaries and across disciplines to overcome technological challenges and to develop new techniques, methods, and better equipment to study the brain. In our study of the top concepts in funded grant awards, research is driven towards a better understanding of diseases and disorders related to Brain and Neuroscience, such as autism and Alzheimer Disease. This is coupled with an emphasis on drug development, for instance in the area of schizophrenia treatment. Strong research is also evident in the area of genes and molecular sequences where concepts such as connectome and transcriptome have either been detected as having rapid growth or are already considered important concepts in Brain and Neuroscience research publications.

By providing the first attempt to understand the overall state of research in Brain and Neuroscience, the report reveals patterns of activities globally, which we hope will be useful to policy makers and decision makers in steering future strategy in Brain research. There is also potential to conduct a deeper analysis of research in specific semantic groups of Brain and Neuroscience research, for example, focusing only on disorders, or chemical and drugs related publications and concepts. Exploring the brain is akin to exploring the mind and exploring the self. Thus, it is with great interest and anticipation that we watch for further developments in this important field of science, which will certainly affect us in one way or another as we learn more about our own brains.

Next, we compared the top concepts within the Brain and Neuroscience research publications from Scopus against publications produced by the recipients of funded grant awards related to Brain and Neuroscience research from the National Institutes of Health (NIH), and project abstracts that were available from the list of brain research projects supported by the European Commission (EC) Concepts were extracted from about 2 million Brain and Neuroscience articles from Scopus, 59,637 articles produced by recipients of funded grant awards relating to Brain and Neuroscience research from NIH, and 136 project abstracts

available from the Brain research projects supported by the EC. As expected, concepts such as "Brain," "Neurons," "Seizures," and "Brain Neoplasms" were seen with similar frequency in the published articles and the NIH-funded grant abstracts. However, concepts such as "Eye," "Pain," and "Stress, Psychological" were more highly represented in published articles than in NIH-funded abstracts, suggesting a divergence from funding to publication.

Not surprisingly, NIH-funded abstracts more often contained disease-related concepts, consistent with the NIH's focus on areas of research with perceived high societal impact. Compared to the research funded by the EC, US research focused on the concepts "Glioma," "Child Development Disorders, Pervasive," and "Bipolar Disorder." Conversely, concepts such as "Memory Disorders," "Vision Disorders," "Myasthenia Gravis," "Hearing Loss," and "Alkalosis" were more frequent in the EC-funded research compared to the US, suggesting a different emphasis in research relating to disorders in Brain and Neuroscience (see Table 2). In the US, drugs related to substance abuse were highly researched, with the appearance of concepts such as "Methamphetamine," "Nicotine," and "Cannabis." In contrast, antipsychotic drugs such as "Risperidone" and "Clozapine" that are mainly used to treat schizophrenia were areas of focus in the EC-funded research