

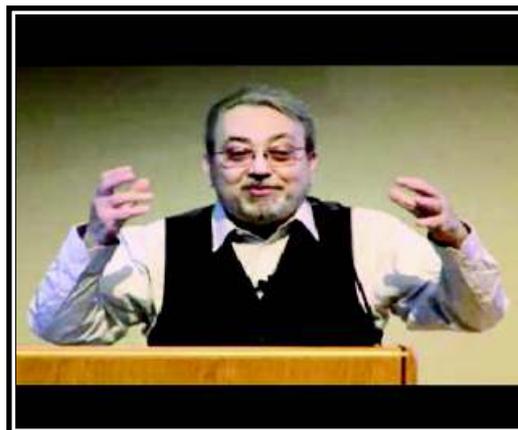
*In the memory of Hagop Souren Akiskal...*

## Opening up new horizons in the field of bipolar disorders: power of observation, research, thinking and creativity

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Psychiatry and the area of bipolar disorders lost a great figure who has expanded our horizon. Hagop S. Akiskal was a good clinician, a good observer, and a creative, humanistic scientist who regarded history and valued novelty, a good friend to many people all over the world, a source of inspiration who opened new horizons in the field of bipolar disorders. I greet his memory and his contributions with deep respect. I am sure that everyone who caught the privilege of knowing him closely, or who had the chance to be among the audience in any of his talks, or who had read and learned his contributions from books and journals share my feelings of respect.



**Hagop S. Akiskal**

16 Ocak 1944 - 20 Ocak 2021

I wonder if there is a colleague who did not hear Akiskal's name, who does not know his extraordinary contributions especially to the field of bipolar disorders. Is it possible to talk about a contemporary and modern classification in the field of bipolar disorders without mentioning his name and his contributions? Is it possible to work on crucial areas pertaining to bipolar disorder such as temperament, subthreshold states, bipolar spectrum, creativity and genetics without following his conceptual footsteps?

Hagop S. Akiskal's name is so much engraved on the minds together with bipolar disorders that I frequently witnessed the astonishment of many colleagues when they heard about his first prominent contribution occurred in the form of an effort to integrate psychoanalytic, behavioural and biological domains in the field of depression. Together with McKinney (1), Akiskal published a review on the perspective that depression occurred as a result of the interaction of genetic, chemical, developmental and interpersonal factors, under the light of current evidence at the time. This was an influential contribution to this important conceptual view of that period. In this integrative model, they attempted to put together

*Hagop S. Akiskal graduated from Beirut American University as a medical doctor in 1969 and immigrated to USA. He obtained his psychiatric training at the Universities of Tennessee, Memphis and Wisconsin, Madison. He was appointed Professor of Psychiatry and Pharmacology at the University of Tennessee.*

*In 1990-1994, he was recruited as the Senior Science Advisor to the Director of the National Institute of Mental Health (NIMH). He founded and directed the International Mood Center at the University of California at San Diego.*

*Since 1996, he was the Editor-in-Chief of the Journal of Affective Disorders (lately Emeritus Editor).*

*He received numerous awards. Some are Gold Medal for Pioneer Research (Society of Biological Psychiatry, USA), Anna Monika Prize (Germany), NARSAD Prize (USA), Jean Delay Prize (World Psychiatric Association), Jules Baillarger Prize (France), Aretaeus Prize (Italy), Ellis Island Honor Medal (USA), Aristotle Gold Medal (European Brain and Behavior Society).*

her psychoanalytic, behavioural and biochemical hypotheses for depression, proceeding from to-date research and observations. Data coming from psychoanalytic model (attachment and disruption of attachment, in other words object loss, leading to depression-like clinical features), behavioural model (loss of reinforcement or loss of control over reinforcement) and biological model (participation of diencephalic reward and reinforcement centers to the process in depression) were reviewed in an integrative manner. I would like to remind that this article was published in 1973. During the following decades, this approach is developed further and enriched with supportive evidence and contributions.

One of early contributions of Akiskal is in the field of the transition from neurotic depression concept to dysthymia. In that era, chronic depressions were considered as neurotic depression and there was prejudice of insufficient treatment response. He addressed the adverse consequences of both of these opinions with his research and articles (2). He joined the group who worked for cleaning chronic depression from the above mentioned stigma and prejudices, and more importantly, supporting the entity's treatability.

Akiskal contributed to many topics in the area of depression and bipolar disorders with research and conceptual approaches. Mixed states, bipolar disorder with anxious features, resistant depression, co-occurrence of personality and mood disorders are among those.

Akiskal's most important and widely influential contributions are on subthreshold states and temperament. His research on cyclothymia opened multidirectional new horizons, provided basis for the inclusion of this diagnosis in official classifications and drew attention to some features, especially affective temperaments, which are precursors of bipolar disorders (3,4). The most important innovative aspect of the horizons that Akiskal opened, via affective temperament concept and his research, is his expansion of the search for understanding bipolar disorders, from the clinical area where it was trapped, towards the field of temperament. Therefore, the area of search was expanded towards the population that was not the focus of attention, for comprehensive research, before. Conceptual and ideational opportunities created by this approach did not turn into research as much as it is expected

yet, especially in genetics. It is possible to say that many problems in the area of genetic research in psychiatry play an effective role in this. Akiskal's frequent statement expresses the extent and value of temperament, subthreshold states and genetics: "A gene or genes cannot be existing only for pathology; cannot be identifying and producing only pathology. Without understanding the importance and engaging the place of genes in the formation of 'normal', it is not possible for us to solve the genetics of illnesses such as bipolar disorder where the genetic aspect is dominant. Temperament (affective temperament) completes the missing link" (5).

When explaining the link between genes, temperament and behaviours, he addressed the issue through features and behaviours like extraversion, assertiveness, innovation, adventurousness, willingness to take risks. He expanded it to evolutionary psychiatry. His frequent example was migration to America. He frequently used the phrase, "Migration is not a random phenomenon". The relationship between evolutionary processes and affective temperament features was an area which Akiskal produced extensive conceptual hypotheses. He attempted to discuss temperamental features brought what kind of adaptive advantages or corresponded with what kind of functions in the evolution of humankind with various hypotheses. According to his hypotheses, anxious temperament may have evolutionary role through some adaptive advantages via altruistic anxiety and worry, cyclothymic temperament via romance and creativity, and hyperthymic temperament via exploration, territoriality and leadership (6).

Akiskal was a very good observer, like Kraepelin whom he valued very much and mentioned in every conference. He developed his studies and conceptualizations on affective temperaments basing on clinical and non-clinical observations. He conducted his most important studies in the Mood Clinic in Tennessee University, Memphis, one of first examples of its kind. He described the basic philosophy of these specialized units as "conducting clinical training and research while offering high quality health service" (7) and constantly encouraged colleagues, working in the area of bipolar disorders, in this direction.

The concept of bipolar spectrum was first used by Kraepelin. Although various bipolar spectrum definitions were proposed in recent years

(3,8,9,10), common opinion is that categorical and dichotomic approach of the third edition of Diagnostic and Statistical Manual of Mental Disorders of American Psychiatric Association (DSM-III) (11) is not inclusive enough, and entities which are in multidirectional and close relationship exist on a continuum.

Akiskal made prominent contributions to the reemergence of spectrum perspective in bipolar disorders, after Kraepelin (3,4). He proposed that unipolar-bipolar dichotomy in DSM-III led to the loss of the inclusiveness of continuum and spectrum perspective which is valuable and thought to fit better to nature. He emphasized that many clinical and subclinical states, frequently seen in the interface of major depression and bipolarity, could not be evaluated because of this approach and he brought the concept of bipolar spectrum forward again. In this regard, he de-scribed “soft” and “hard” bipolar phenotypes and expanded the boundaries especially towards “subthreshold bipolarity”. He was criticized by some, for the degree of his speculations, e.g. his attempt to develop the notion of spectrum by halves of numbers. He answered these in advance in his article (12): “The prototypes provided should be seen as an attempt to map this vast clinical territory, rather than as definitive subclassification of bipolar spectrum disorders.”

Some of Akiskal’s creative and innovative perspectives and propositions await further development with further research and evidence. This need gives a task to the researchers who are inspired by creative, pioneering and visionary scientists like Akiskal and Angst and who wish to carry the field further.

Hagop Akiskal was appreciated and admired by numerous people in many countries not only with his observations, studies and conceptualizations, but also with his conferences and presentations. In addition to the content, he filled the meeting rooms with his sincere, colorful, lively, interactive, joyful style, in many countries including Turkey.

Akiskal’s making many friends in Turkey started in the first International Bakırköy Days (1990). Words he expressed there and then were very powerful: “If you wish, import everything from America except two things: fast food and borderline personality disorder diagnostic category...” The discussion he started with this sentence was

pointing at the enriching aspect of looking with a different and critical eye rather than accepting a view without reservation, even if it comes from leading countries and institutions, even if it is widely applied.

Later he made two breathtaking presentations in the National Congress of Psychiatry in Ankara (1992), hosted by Hacettepe University Psychiatry Department and Professor Orhan Öztürk. The first one was New studies and clinical applications in affective disorders and the second one was Emotional life of blues musicians. His musical scientific presentation was a recital that reached from temperament to bipolar disorder, from genetics to the curing effect of art, which was enriched by research they had conducted with his wife Kareen Knarig Akiskal and segments from lives of blues musicians. Hagop Akiskal’s conversation with Yaşar Kemal who was another guest and keynote speaker of the congress during dinner was like the dessert after a feast.

Akiskal’s next stop in Turkey was Ephesus Bipolar Disorder days (1998) in Kuşadası hosted by Dokuz Eylül University Psychiatry Department and Professor Zeliha Tunca. Presence of two prominent names of bipolar spectrum perspective, Akiskal and Koukopoulos made a mark together with Ephesus antique city. Number of stimulating sessions again inspired many colleagues. In a Meet the Expert session, Akiskal’s question and the significance of its verbalization “How would you treat if it was your brother in bipolar depression?” and the interactive discussion became a life time powerful voice in the ears of many participant clinicians.

One of the most important meetings Akiskal attended and supported was Psychiatric Association of Turkey’s first international congress, ‘International Conference on Mood Disorders / Close Encounters of Three Seas: Building Regional Bridges’. It took place in Istanbul in 2006. I had the honor of serving as the scientific program secretary while Psychiatric Association of Turkey Mood Disorders Section organized the meeting and carried the responsibility of scientific program.

In addition to extremely high scientific level, hosting a substantial number of participants, an outstanding aspect of this meeting was composition of speakers and participants. We hosted

speakers and participants from or originated from each of every neighboring country of Turkey. This congress was an example that scientific meetings can also serve peace and friendship. Names of participant countries are the best indicator: Armenia, Azerbaijan, Bulgaria, Cyprus (Turkish Republic of Northern Cyprus and South Cyprus), Georgia, Greece, Iraq, Iran, Israel, Romania, Russia, Serbia-Montenegro, Syria and Turkey.

“Building Regional Bridges” phrase was proposed by Akiskal and accepted without hesitation. We witnessed many times his sharing of his complements whenever he met a colleague from Turkey on this conference’s meaning and value. Akiskal provided his support for this meaningful meeting and inspired our colleagues who came from all neighboring countries.

Every time Akiskal came to Turkey, he regarded to be with all his friends and build human relationship. He always called or visited his Armenian colleagues and friends and refreshed his warm human relations. He met Hrant Dink at one time and mentioned him thereafter movingly, during conversations about friendship. Unfortunately, we were all shocked to lose him by a heartbreaking assassination, shortly after they first met. Hagop, his wife Kareen and all of us were deeply shaken. We shared the agony of this loss, which is great and all of ours, still squeezing our hearts.

I had the chance to work with Akiskal for one and a half months in International Mood Clinic

in San Diego. We started working both on the study of translation and adaptation of TEMPS-A (the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version) to Turkish (13) and on the drafts of several research studies on affective temperaments (14) that we would do in Turkey. This was a time when our friendship with Hagop and his wife Kareen who was also his co-researcher in studies on art and creativity. Both gave a special value to colleagues from Turkey and existence of their many mutual friendships in Turkey is not surprising.

On January 10, 2021, we lost a wise, scope-wide-ning person that we valued much, a source of inspiration, a friend. We lost a teacher who gave special importance to being a clinician and underlined observation; who was courageous and generous in coming up with innovative and creative perspectives and hypotheses from observation and research; who impacted our view on bipolar disorders. We lost a scientist. We lost a good person who had friends in numerous countries.

We are deeply saddened... We will miss him much...

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\*Türkiye Psikiyatri Derneği ve TPD-Duygudurum Bozuklukları Çalışma Birimi'nin düzenlediği Uluslararası Duygudurum Bozuklukları Konferansı / Üç Denizin Buluşması: Bölgesel Köprüler Kurmak başlıklı kongreden birkaç fotoğraf...



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