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BIPOLAR DISORDERS AND BIPOLARITY: THE NOTION OF THE "MIXITY"

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SUMMARY

The notion of "mixity" of the dysphoric phases of the bipolarity includes the most insidious symptoms of the bipolar spectrum of mood disorders: the overlapping between depression-restlessness-irritability-grief-tension-anxiety can cause worsening of the mood disorders and in the most acute phases may cause increased risk of major behavioural disruption including murder and suicide. The early utilization of the rating scale on mixed states, "GT-MSRS", which can demonstrate the level of "mixity" of the mood disorder, can prevent this.

Key words: *bipolar spectrum disorders – early diagnosis – mixed states – mixity - mixed state rating scale – GTMSRS*

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INTRODUCTION

The dysphoric component of mood (mixed states) is quite frequent among all the subtypes of the bipolar spectrum. Mixed states include approximatively 30% of all mood spectrum disorders (Tavormina 2010, 2013, Akiskal 2000, Perugi et al. 2014), however, they are pathologies which are often underestimated or, worse, not diagnosed or treated inappropriately (Agius 2007, Tavormina 2007, 2018).

Emil Kraepelin was among the first psychiatric nosologists who described the mixed states. In his 1921 treatise “Manic-Depressive Insanity” Kraepelin stated that "very often we meet temporarily with states which do not exactly correspond either to manic excitement or to depression, but represent a mixture of morbid symptoms of both forms of manic-depressive insanity". He thus specified six types of mixed states, based on various combinations of manic and depressive mood, thought, and behaviour. These were: depressive or anxious mania, excited depression, mania with poverty of thought, manic stupor, depression with flight of ideas, and inhibited mania.

As we can see, Kraepelin’s description is absolutely correct, so that the modern classifications of the bipolar disorders and mixed states are similar (Akiskal 1996, 2000, Tavormina 2007) (Tables 1, 2).

As Akiskal wrote, the depressive expressions of bipolar disorders have long been neglected; it is crucial to exam the different clinical expressions of bipolar depression including, among others, retarded depression, agitated and/or activated depression, mood-labile depression, irritable-hostile depression, atypical depression, anxious depression, depressive mixed state, and resistant depression (Akiskal 2005).

Clinicians find great difficulties in making a correct diagnosis of the mood disorders which they are assessing, above all when mixed states are present: this is because the patients mainly focus their own symptoms on depressive uneasiness (inducing the clinicians to frequently prescribe antidepressants drugs alone or together with benzodiazepines), inducing them to prescribe these inadequate treatments and not take note of the real problem of increasing dysphoria caused by these treatments (Tavormina 2018).

CLINICAL CONSIDERATIONS

The following are the main symptoms of the mixed states are (Tavormina & Agius 2012): depressed mood together with irritability, anhedonia and widespread apathy, reduced ability to concentrate and mental over-activity, a sense of despair and suicidal ideation, hyper/ hypo- sexual activity, insomnia, comorbidity with anxiety disorders (PAD, GAD, OCD, soc ph.), various somatisation symptoms (mainly: gastrointestinal disorders, headaches), disorders of appetite, substance abuse (alcohol and/or drugs), delusions and hallucinations, antisocial behaviour. At least two or more of them need to be present (Tavormina & Agius 2012). How many times the news we can hear or read contains reports of murders, murders-suicides, familiar massacres, rapes, substance abuse connected with violence, etc.: very often a bipolar mood disorder illness, untreated or mistreated, is responsible of these facts.

The “mixity” of depressive phases (that are the most insidious symptoms of overlapped depression-restlessness-irritability) can cause increased risk of suicidality (Akiskal 2007): the intensity of these symptoms can be shown using the rating scale for mixed states “GT-MSRS”, (Tavormina 2014), an easy rating scale to administer to the patient structured in eleven items (and 7 sub-items), to demonstrate the level of the mixity (a score from 2 to 6: medium-light level; a score from 7 to 12: medium level; a score from 13 to 19: high level); (Tavormina 2014, 2015).

METHODS

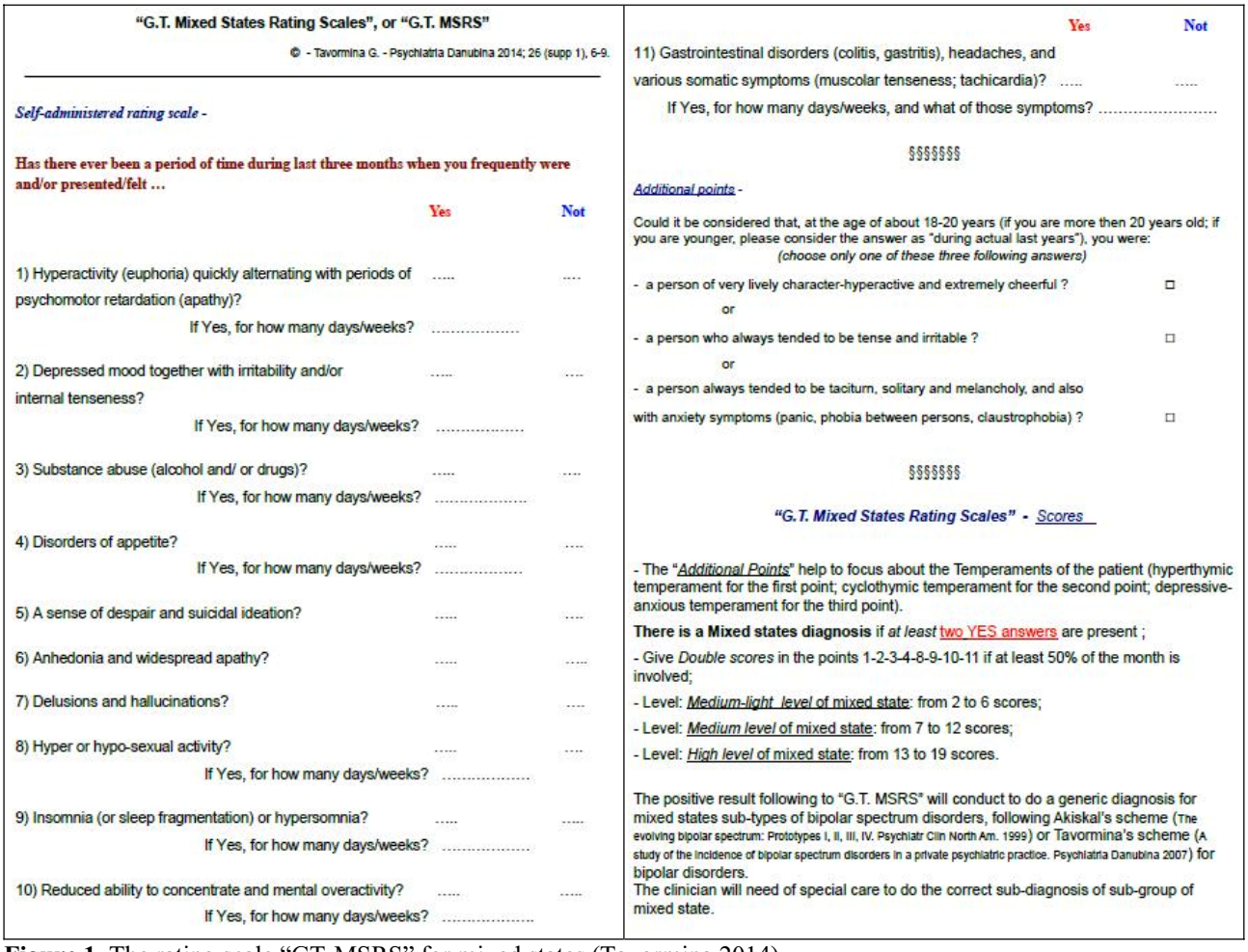
All the points of mixity symptoms are contained inside the rating scale “GT-MSRS”, structured in eleven items, eight of them subdivided in sub-items (Tavormina 2014) (Figure 1).

Table 1. Akiskal's schema of bipolar spectrum (Akiskal & Pino 1999)

Bipolar ½: schizobipolar disorder
Bipolar I: core manic-depressive illness
Bipolar I½: depression with protracted hypomania
Bipolar II: depression with discrete spontaneous hypomanic episodes
(*Bipolar II, "sunny" bipolars* - hypomanic periods (2-3 days) characterized by cheerfulness and jocularity, people-seeking, increased sexual drive and behavior, talkativeness and eloquence, confidence and optimism, disinhibition and carefree attitudes, reduced sleep need, eutonia and vitality, and over-involvement in new projects).

Bipolar II½: depression superimposed on cyclothymic temperament
(*Bipolar II½: Unstable, "darker" BP II* - dysphoric, irritable hypomania superimposed upon an inter-episodic cyclothymic temperament ("roller-coaster" course often misinterpreted or misdiagnosed as borderline personality disorder). Often comorbid with panic disorder and social phobia, as well as, bulimia and borderline personality disorder).

Bipolar III: depression with induced hypomania (i.e., hypomania occurring solely in association with antidepressant or other somatic treatment)
Bipolar III½: prominent mood swings occurring in the context of substance or alcohol use or abuse
Bipolar IV: depression superimposed on a hyperthymic temperament
(*Bipolar IV: VERY DANGEROUS condition* - depression superimposed on a stable hyperthymic temperament: exuberant, articulate and jocular, overoptimistic and carefree, overconfident and boastful, high energy level, full of plans and activities, ... with broad interests, over involved, uninhibited and risk-taking, and an habitual short sleeper. And suddenly slip into deep (often) treatment-resistent depression. This is an extremely DANGEROUS condition because hyperthymic individuals are intolerant of any degree of depression, and certainly poorly tolerate the affective dysfunction associated with a depressive mixed state. Many mysteries about suicide, and suicides that one reads about in the newspaper (ie, "an extremely successful and happy person, who had everything, put the gun in his mouth") may well belong to this category).



"G.T. Mixed States Rating Scales", or "G.T. MSRS"

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Self-administered rating scale -

Has there ever been a period of time during last three months when you frequently were and/or presented/felt ...

	Yes	Not
1) Hyperactivity (euphoria) quickly alternating with periods of psychomotor retardation (apathy)?	.....	....
If Yes, for how many days/weeks?		
2) Depressed mood together with irritability and/or internal tenseness?	.....	....
If Yes, for how many days/weeks?		
3) Substance abuse (alcohol and/ or drugs)?	.....	....
If Yes, for how many days/weeks?		
4) Disorders of appetite?	.....	....
If Yes, for how many days/weeks?		
5) A sense of despair and suicidal ideation?	.....	....
6) Anhedonia and widespread apathy?	.....	.....
7) Delusions and hallucinations?	.....	....
8) Hyper or hypo-sexual activity?	.....	....
If Yes, for how many days/weeks?		
9) Insomnia (or sleep fragmentation) or hypersomnia?	.....	.....
If Yes, for how many days/weeks?		
10) Reduced ability to concentrate and mental overactivity?	.....	.....
If Yes, for how many days/weeks?		

	Yes	Not
11) Gastrointestinal disorders (colitis, gastritis), headaches, and various somatic symptoms (muscolar tenseness; tachicardia)?	.....	.....
If Yes, for how many days/weeks, and what of those symptoms?		

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Additional points -

Could it be considered that, at the age of about 18-20 years (if you are more then 20 years old; if you are younger, please consider the answer as "during actual last years"), you were:
(choose only one of these three following answers)

- a person of very lively character-hyperactive and extremely cheerful ? ☐
or
- a person who always tended to be tense and irritable ? ☐
or
- a person always tended to be taciturn, solitary and melancholy, and also with anxiety symptoms (panic, phobia between persons, claustrophobia) ? ☐

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"G.T. Mixed States Rating Scales" - Scores

- The "*Additional Points*" help to focus about the Temperaments of the patient (hyperthymic temperament for the first point; cyclothymic temperament for the second point; depressive-anxious temperament for the third point).

There is a Mixed states diagnosis if *at least* two YES answers are present ;

- Give *Double scores* in the points 1-2-3-4-8-9-10-11 if at least 50% of the month is involved;
- Level: *Medium-light level* of mixed state: from 2 to 6 scores;
- Level: *Medium level* of mixed state: from 7 to 12 scores;
- Level: *High level* of mixed state: from 13 to 19 scores.

The positive result following to "G.T. MSRS" will conduct to do a generic diagnosis for mixed states sub-types of bipolar spectrum disorders, following Akiskal's scheme (The evolving bipolar spectrum: Prototypes I, II, III, IV. Psychiatr Clin North Am. 1999) or Tavormina's scheme (A study of the incidence of bipolar spectrum disorders in a private psychiatric practice. Psychiatria Danubina 2007) for bipolar disorders.
The clinician will need of special care to do the correct sub-diagnosis of sub-group of mixed state.

Figure 1. The rating scale "GT-MSRS" for mixed states (Tavormina 2014)

Table 2. Tavormina's schema of bipolar spectrum (Tavormina & Agius 2007)

	Acute mania
1 - Bipolar I	(→ dysphoric mania)
2 - Bipolar II	(→ rapid cycling bipolarity, mixed disphoria)
3 - Cyclothymia	(→ rapid cycling bipolarity)
4 - Irritable Cyclothymia	(rapid cycling bipolarity)
5 - Mixed Dysphoria	(depressive mixed state)
6 - Agitated Depression	(→ depressive mixed state)
7 - Cyclothymic temperament	(→ Mixed Dysphoria, depressive mixed state, rapid cycling bipolarity, agitated depression, bipolar I-II)
8 - Hyperthymic temperament	(→ Agitated Depression, Irritable Cyclothymia, bipolar II)
9 - Depressive temperament	(→ brief rec. depr, agitated depression)
10 - Brief recurrent depression	(→ dysthymia, major depressive episode, agitated depression)
	Unipolar Depression

The presence of hyperactivity (or euphoria) quickly alternating with periods of apathy (or psychomotor retardation) is the matter of the first item; these symptoms are frequently present in the diagnosis of rapid cycling bipolarity and irritable cyclothymia. The presence of depressed mood overlapped with irritability and/or internal tenseness is the matter of the second item; these symptoms are frequently present in the diagnosis of mixed dysphoria and agitated depression. The presence of substance abuse (alcohol and/or drugs)and disorders of appetite are the matters of the third and fourth items: these symptoms are usually present in very unstable mood diagnosis (mixed dysphoria, agitated depression, irritable cyclothymia). Anhedonia and widespread apathy, and a sense of despair with suicidal ideation (5^{th} - 6^{th} items), are frequently present in the depressive phases of the instability (agitated depression; recurrent depression). Delusions and hallucinations (7^{th} item), less frequent then other symptoms, might be found in all type of mood disorder mixed states. The presence of hyper-sexual activity or hypo-sexual activity are typical of the dysphoric-hyperthymic phases of the mood (the hyper-sexual activity) or of the depressive-agitated phases of the mood (the hypo-sexual activity). In the 9^{th} item we find the insomnia (or sleep fragmentation), usually present in the agitated phases of the mood (mixed dysphoria, agitated depression, irritable cyclothymia) and instead the hypersomnia is typical of the depressive-agitated phases of the mood (recurrent depression, cyclothymia, agitated depression). The presence of mental overactivity and the reduced ability to concentrate (10^{th} item) are the most typical symptoms of all mood mixed states diagnosis: these symptoms will be reduced by mood-stabilisers and then may disappear when the patients go into recovery. The last item is the 11^{th}, the presence of somatisations (gastrointestinal disorders, such as colitis and gastritis; headache; muscular tenseness; tachycardia; atypical dermatological problems), in several conditions these may be the main clue which could help the psychiatrist to identify mixed states early, so that the clinician can diagnose them correctly and quickly.

The four diagnoses of "Recurrent Depression" and "Major Depression" emerged in the first validation study on "GT-MSRS" (Tavormina 2015) scored within the "medium level" of this rating scale, showing how the symptoms of mixity (in these examples: anhedonia; insomnia/hypersomnia; mental overactivity; hypo-sexual activity; sense of despair; somatisations) are diffused within all mood disorder sub-types, including "Recurrent Depression" and "Major Depression". In consequence of this, the prescription of mood stabilisers together with antidepressants, even in patients with a diagnosis of major depression or recurrent depression, is crucial for a good treatment.

FINAL EVALUATIONS AND CONCLUSIONS

Very often patients with bipolar disorders received a correct diagnosis after on average 25 years of illness (McCombs et al. 2007, McCraw et al. 2014, Akiskal-Benazzi 2005, Tavormina 2018). Clinicians find great difficulty in making a correct diagnosis of the mood disorders which they are assessing, above all when mixed states are present: this is because the patients mainly focus their own symptoms on depressive uneasiness, inducing the clinicians to frequently prescribe inadequate treatments such as antidepressants drugs alone or together with benzodiazepines, thus increasing dysphoria (Tavormina 2016, Agius et al. 2007). A correct approach to the diagnosis of bipolarity can be done using the rating scale "GT-MSRS".

The following significant sentence of Hagop Akiskal (from the Conference: "Melancholia: beyond DSM, beyond neurotransmitters" – May 2–4, 2006, Copenhagen) needs to be reflected on: "Melancholia as defined today is more closely aligned with the depressive and/or mixed phase of bipolar disorder. … Given the high suicidality from many of these patients, the practice of treating them with antidepressant monotherapy needs re-evaluation".

And also: mixed states occur in an average of 40% of bipolar patients over a lifetime; current evidence supports a broader definition of mixed states consis-

ting of full-blown mania with two or more concomitant depressive symptoms (Akiskal et al. 2000).

All this means is that it is essential to remark once again what has been described in previous papers: that the "instability of mood", more than the "depression", is the main issue which the clinician needs to deal with in a patient with mood disorder; this relates to the important notion, that the depressive episode is only one phase of a broader "bipolar spectrum of mood" (Tavormina 2007, 2012, Akiskal 2000). In consequence of this, when considering bipolarity the notion of the mixity becomes the conceptual reference point of the diagnostic process.

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