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Abstract

Background: The boundaries between mood states in bipolar disorders are not clear when they are associated with mixed characteristics. This leads to some confusion to define appropriate therapeutic strategies. A dimensional approach might help to better define moods states in bipolar disorders and may be use as an indicator of the response to treatment.

Therefore, we proposed a new tool based on a dimensional approach, built with a priori five sub-scales and focus on emotional reactivity rather than exclusively on mood tonality. This study was designed to validate this MAThyS Scale (Multidimensional Assessment of Thymic States).

Method: One hundred and ninety six subjects were included: 44 controls and 152 bipolar patients in various states: euthymic, manic or depressed. The MAThyS is a visual analogic scale consisting of 20 items. These items corresponded to five quantitative dimensions ranging from inhibition to excitation: emotional reactivity, thought processes, psychomotor function, motivation and sensory perception. They were selected as they represent clinically relevant quantitative traits. **Results**: Confirmatory analyses demonstrated a good validity for this scale, fair convergent and divergent validity (multi-traits multi-method analyses), a good internal consistency both at a global and a dimensional level (Alpha Cronbach ranging from 0.70 to 0.93). The MathyS scale is moderately correlated of both the MADRS scale (depressive score; $r = -0.45$) and the MAS scale (manic score; $r = 0.56$). Some dimensions were linked (emotional reactivity and thought processes, $r = 0.71$; psycho-motricity and motivation, $r = 0.70$). Exploratory analyses: Horn procedure is in favour of 2 dimensions. Using this procedure the first eigen value explains by its own 42% of the total variance of the 20 items while the second eigen value explains only 8.8% of this variance. The factor analysis with varimax rotation conducted on the 2 factors solutions separated clearly the items related to emotional reactivity to other items defining a global functioning based on an inhibition/activation process

Conclusions: The two-dimensional model helps identify two very robust dimensions, namely emotional reactivity and the global score, with a very high psychometric validity. The characterisation of bipolar mood states based on a global score assessing inhibition/activation process associated with emotional reactivity (rather than the classical opposition euphoria/sadness) can be useful to order thymic states on a continuum and define a spectrum of mixed states.

Key words: bipolar disorder, manic state, depressive state, dimensional approach, self-questionnaire.

Introduction

The heterogeneity of mood episodes is a crucial issue especially in bipolar disorders and leads often to some confusion in diagnostic and therapeutic strategies. Apart from the classical syndromes characterizing euphoric mania and melancholic depression, recent literature has pointed to alternative mood states associating both manic and depressive symptoms. This resulted in the definition of various syndromes including mixed states, dysphoric mania (McElroy et al., 1992), agitated depression (Koukopoulos, 1999), depressive mixed state (Benazzi et Akiskal, 2001; Benazzi, 2003) and more recently mixed hypomania (Akiskal et Benazzi, 2005; Suppes et al, 2005). As a consequence, this leads to question the best therapeutic strategies (Akiskal et al, 2005). As the boundaries between the various states associating both depressive and manic symptoms have yet to be clarified, there is a need to explore whether dimensional approaches could help to refine their definitions (McElroy et al., 1992; Bauer, 1994; Biondi et al., 2005).

With a very modern point of view, Kraepelin (1921) defined mood states as originating from the excitement or inhibition of the three domains of the psyche: cognitive processes (train of thought rather than its contents), mood, and volition (expressed in psychomotor activity). We have extended this notion, by replacing mood tone (euphoria vs. sadness) by emotional reactivity (hyporeactive vs. hyperreactive), which is closer to the concept of dimensions, as it may be considered a quantitative symptom. An emotion is characterized not only by its tone (pleasant/unpleasant), but also by its intensity or reactivity. In concrete terms, all depressive states are characterized by sadness, so affective mood tone cannot distinguish between different types of depression. However, the quantitative component of emotions can provide a useful discriminatory element. Indeed, emotional reactivity can be inhibited, leading to a loss of pleasure or anhedonia, which, in its most complete expression, results in true emotional anesthesia. Kraepelin (1921) described certain depressive patients as insensitive even to bad news. Such emotional anesthesia was also described by Goodwin and Jamison (1990) in traditional slowed down depressions. However, some bipolar depressions with atypical features are not characterized by an emotional hyporeactivity. Conversely, manic and mixed states were found to be better characterized by emotional hyperreactivity than by affective tone, which is very variable (Henry et al., 2003). Emotional hyperreactivity implies that emotions are felt with a greater intensity than usual

and that they vary according to environmental stimulations. Thus, emotional reactivity might be useful to discriminate states with mixed features.

Based on these concepts we developed a tool called MAThyS (Multidimensional Assessment of Thymic States). This is a visual analogic scale based on a dimensional approach aiming to discriminate between different sub-populations among patients suffering from bipolar disorders. The instrument is designed as a multi-dimensional assisted self-administered questionnaire comprising 20 items relating to individual states as perceived by patients for the preceding week. Each item is set out as a continuous measure in the form of a visual analogic scale of 10 cm on which the subject is asked to make a mark to indicate where he/she is positioned between the two predefined extreme propositions.

The scale is developed using five *a priori* dimensions which can fluctuate from inhibition to excitation to explore mood episodes and represent quantitative dimensions (see annex). The five dimensions are: emotional reactivity, cognition speed, psychomotor function, motivation and sensory perception. Because the dimensions assess inhibitory or activation processes, they can be applied to manic or depressive states as well as to states presenting with an admixture of both. Emotional reactivity may be considered as a new component in comparison of current mood scales and seems appropriate to define mixed states.

The objective of MAThyS is to define bipolar mood states as a function of an inhibition/activation process using a dimensional approach. According to this concept, mood is defined using emotional reactivity rather than tonality of affects. This approach can help to order bipolar mood states on a continuum and to define a spectrum of mixed states.

The aim of the study is to present elements of validation of the MAThyS Scale (Multidimensional Assessment of Thymic States), with an account of the reliability, construct validity and divergent validity of this assisted self-administered questionnaire.

Method

Subjects

The first group included control subjects, without bipolar disorder, recruited by means of an advertisement (for example in shopping areas and in sportive associations). Normothymic bipolar outpatients were recruited from a specific consultation, and bipolar patients presenting with a depressive, manic, hypomanic or mixte episodes were recruited from consecutive admissions as inpatient in a unit of general psychiatry and as outpatients in a consultation for bipolar disorders corresponding to a specific geographic area and thus very representative of a general population of bipolar patients (Charles Perrens Hospital, Bordeaux, France).

Patients and controls were interviewed by a trained psychologist using the section of mood disorders of the French version of the Diagnosis Interview for Genetic Studies (Preisig et al., 1999) providing DSM-IV diagnosis (APA, 1994). Subjects with current alcohol or substance misuse were excluded patients according to the DSM-IV criteria. For inclusion in the group of normothymic bipolar patients, subjects did not, at the time of the evaluation, fulfill the criteria for a major depressive episode or a manic, mixed or hypomanic episode, according to DSM-IV criteria. Normothymia was confirmed by a general clinical evaluation, carried out by the treating psychiatrist, and by low scores on depressive and manic scales (MADRS≤12 and MAS≤4) (Montgomery and Asberg, 1979; Bech et al., 1978). Patients were included after giving informed consent and did not receive any financial compensation (controls and bipolar patients). The study was approved by the Ethics Committee.

MAThyS scale

Administration of the scale

MAThyS is a self-completed questionnaire filled in with assistance at least for the first completion. The evaluation concerns mood during the last week. Because it is a visual analogic scale, the patient must choose between the two proposed statements for each item and then indicate, with a vertical line, his or her state. When the patient is in is basal state, the vertical line should be marked in the centre of the horizontal line between the two proposed statements. The marking of the vertical line in this position indicates no change from the basal state. By contrast, if the patient's mood fluctuates, he or she should decide which of the two

proposed statements best describes his or her current state. The vertical line should then be marked between the centre and the selected statement, the precise position with respect to the extremity of the horizontal line depending on the extent to which the patient identifies with the statement. The time to fill in the MAThyS is about 10 mns

Scoring

Score is determined line-by-line and varies from 0 to 10 for each line. A score of 0 corresponds to inhibition of the state evaluated by the item. A score of 5 indicates no change from the patient's usual state and a score of 10 corresponds to excitation for the evaluated state. An overall score of between 0 and 200 is thus obtained. This scale is not devoted to make a diagnosis of mood state but allow to determine 1) the general level of inhibition/activation processes (lower scores indicate general inhibition and higher scores indicate general excitation; 2) the state of emotional reactivity (hyporeactive/herperreactive). The measure is the number of centimetres from the left hand anchor. Items measured from 0 to 10 are: 1; 2; 3; 4; 11; 12; 13; 14; 15; 16; 19; 20 and items measured from 10 to 0 are : 5; 6; 7; 8; 9; 10; 17; 18. The subscore for emotional reactivity is obtained by the sum of items: 3; 7; 10; 18. A verbatim and a guidebook are available and can be provided by the corresponding author.

Statistical analyses

First a descriptive analysis of items explored their distribution (missing data, normality, scatter of responses, floor and ceiling effects) and redundancy (estimation of Pearson's correlation coefficient between items two by two, with a threshold at 0.70). Following this, convergent validity was explored using the multitrait multimethod analyses (MTMM) to confirm the assumed subscale structure. This procedure is carried out to ensure that each item is strongly correlated with the scale to which it is assumed to belong (with a correlation coefficient over 0.40), the score of the subscale being calculated without the item considered. This step also assess whether the items are more strongly correlated with the scale to which they belong (again without the item of interest) than with other subscales in the instrument. The internal consistency of each subscale was then estimated with the Cronbach

Alpha coefficients and their 95% confidence intervals estimated using a bootstrap procedure. Finally, elements of convergent and divergent validity were assessed by comparing the MAThyS to the MADRS and the MAS.

If the predetermined structured of the MAThyS was not confimed by the MTMM analysis, a traditional exploratory psychometric analysis was planned (Falissard et al., 2001). The screeplot of the correlation matrix of the 20 items was drawn, the number of dimensions of the scale was appreciated with application of Kaiser's criterion (eigenvalues>1) or Horn procedure (random simulations of data sets), a series of maximum likelihood factor analyses (FA) with varimax rotations (an analysis with promax rotations gave very close results). All these analyses were conducted using the programme R 1.8.0 (Falissard, 2004).

Results

Sample characteristics

The sample of 196 subjects was composed of 61 (31.12%) men and 135 (68.88%) women, with a mean age at interview of 38.36 (±12.75) years.

Seventy one (36.22%) patients had always been single, 85 (43.37%) patients were married or in cohabitation, and 39 (19.9%) were separated or widowed. Most patients presented type I bipolar disorder 92 (60.53%). The repartition in each group is summarized in table 2.

Acceptability

Only one subject in the group of depressive patients and eight in the "manic" group (including hypomanic and mixed states) did not complete the questionnaire, which means that the participation rate is satisfactory for both these groups at 96.4% and 86.3%. The total number of questionnaires filled is thus equal to 187.

All respondents completed all items in the scale (no missing data), which is in favour of good acceptability of the instrument, and suggests it was well understood and easy to complete.

Item analysis

This analysis was conducted on the whole sample population. In average, the responses were towards the centre of the visual analogic scales, the mean for each item being around 5 (range 4.43 to 6.33). This observation could be linked to the instructions provided, which indicate that "the centre of the line presents your usual state". The dispersion of responses is also similar from one item to another (standard deviation between 1.96 and 2.89). Neither floor nor ceiling effects were observed in the population overall.

Considering the threshold chosen, the item correlation matrix of MAThyS only shows high correlations between two pair of items: items 7 and 18 in the hypothesised dimension "emotional reactivity" (r=0.75), and items 15 and 16 in the dimension "motivation" (r=0.80). Thus inter-item redundancy is low in the instrument overall.

Multi trait multi method analysis

For the population overall, all correlation coefficients of items with their respective hypothesised scales were above 0.40. However, some items are not optimally correlated with the subscale to which they were expected to belong.

Three items theoretically connected with the scale "cognitive speed" are equally or more correlated with other scales: item 5 (attention/distraction in relation to the environment, r=0.41) with the scales "emotional reactivity" (r=0.42), "motricity" (r=0.42), and "sensory perception" (r=0.42); items 12 (ideo-motor slowing/acceleration, r= 0.44) with "emotional reactivity" (r=0.60) and "psychomotor function" (r=0.54); and item 14 (desire to communicate with others, r=0.47) with "emotional reactivity" (r= 0.48), "motivation" (r=0.59) and "sensory perception" (r=0.50).

Likewise, items 1 (sensitivity to colour) and 8 (sensitivity to music), theoretically belonging to the "sensory perception" scale (r=0.44 and 0.58), correlate better with, respectively, the scales "motivation (r=0.49) and "emotional reactivity" (r=0.61). Finally, item 11 (feeling energetic) hypothesised as belonging to the scale "motricity" (r=0.63) is more strongly linked to the scale "motivation" (r=0.70), and item 4 (withdrawal, de-inhibition), theoretically belonging to the "motivation" scale (r=0.55) is better correlated with the "cognitive speed" scale (r=0.57).

It is noticeable that items of the "emotional reactivity" subscale are all consistently more correlated to their own scale than to the other subscales.

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Internal consistency of hypothesised subscales or dimensions of MAThyS

The analysis of internal consistency of MAThyS subscales shows high Cronbach alpha coefficients, all equal or above the selected threshold of 0.70 (Table 4).

Analysis of inter-scale correlations

Two high correlations were observed between subscales (table 4). Thus the subscales "emotional reactivity and "cognitive speed" on the one hand, and "motricity and "motivation" on the other are strongly linked (r= 0.71 and 0.70 respectively). The correlation coefficients between the scores of all the subscales and the total MAThyS score (omitting the subscale under consideration, according to MTMM procedure) are high (r=0.68 to 0.79), which is in favour of global internal consistency of the scale.

External validity

Table 3 gives an overview of the characteristics of the population as a whole and group by group. We excluded in this analysis the patients with mixed features in order to have means for pure depressive (supposed to have the lowest scores) and manic states (supposed to have the highest scores). Controls and normothymic bipolar subjects have similar scores close to the theorical mean of 100 (100.5 for controls, 102.0 for normothymic bipolar subjects). Depressed patients show low scores in all dimensions while the contrary is observed for manic or hypomanic patients.

The MathyS scale is moderately correlated of both the MADRS scale (depressive score; r = -0.45) and the MAS scale (manic score; r = 0.56).

Following this first phase, the decision was made to pursue psychometric analyses using an exploratory procedure.

Exploratory psychometric analyses

Since the MTMM analysis does no confirm unequivocally the a priori structure of the MAThyS; exploratory analyses were done as planned in the statistical section.

The screeplot of the correlation matrix of the 20 items is presented figure 1. Kaiser's criterion leads to retain 4 dimensions while Horn procedure is in favour of 2 dimensions. Using this procedure the first eigen value explains by its own 42% of the total variance of the 20 items while the second eigen value explains only 8.8% of this variance.

The factor analysis with varimax rotation conducted on the 2 factors solutions separated clearly the items related to emotional reactivity to other items defining a global functioning based on an inhibition/activation process (Table 5).

Discussion

The descriptive analyses are in support of a good acceptability. In addition, redundancy between items is low. Concerning the external validity, the contrasted groups constituting the studied sample have scores compatible with their clinical characteristics. Moreover MAThyS scale indicate moderated and coherent links with the MADRS and MAS scales.

The MTMM analysis cast a doubt on the robustness of the predetermined structure of the MAThyS. If the reliability of the subscales is good, several items are more strongly correlated with one or several subscales other than their own. Moreover, the factor analysis with 5 factors do not lead to an interpretable solution.

This entails reconsideration of the structure of the MAThyS scale. Since a first component explains an important amount of variance, the 20 items may be summed which lead to an indicator of a global inhibition (low score) or a global activation (high score). Low score to emotional reactivity should allow to discriminate state with emotional hypo-reactivity from mood states with emotional hyper-reactivity whatever to tonality of mood. The scale can be implemented to obtain a total score enabling comparison of the state of a patient over time. When the subject starts a thymic episode, the MAThyS score will vary according to his/her thymic state, upwards in a state of exaltation and downwards in a state of inhibition. When the episode resolves, the score will tend towards the mean (100).

The subscale "emotional reactivity" appears consistent either according the MTMM or the 2 factor analysis. Hence, the sum of the item 3, 7, 10 and 18 may be used to assess this construct.

There are some limitations and advantages for this scale. This scale was not contruct on a classical model because the normal state (corresponding to normothymic state) is between two pathological states. This particular construction is due to the possible fluctuation

of the mood in two opposite ways. The advantage of a visual analogic scale is that subjects don't have to make binary decisions, or to refer to a norm. The self-administered questionnaire is assisted (a verbatim and a guidebook are available and can be provided by the corresponding author) in order to help clinician to use the scale.

Preliminary results using this scale have showed that a dimensional approach using a global score based on inhibition/activation process associated with emotional reactivity seems appropriate to define a broad mixed state spectrum including a relevant number of patients who would be diagnosed of major depression according to DSM-IV (Henry et al., in press). Moreover, bipolar depressive states are not homogeneous and this dimensional approach is useful for discriminating the different forms of bipolar depression. Bipolar depressions may be classified as hypo-reactive or hyper-reactive. This classification might have therapeutic implications because hyper-reactive depression with a moderate global score should belong to the broad spectrum of mixed states (Henry et al., in press).

The characterisation of bipolar mood states based on a global score assessing inhibition/activation process associated with emotional reactivity (rather than the classical opposition euphoria/sadness) can be useful to order thymic states on a continuum and define a spectrum of mixed states. Currently, the other proposition is to define this spectrum based on a categorical approach consisting in counting manic and depressive symptoms (Benazzi, 2003). A dimensional approach could be more appropriate to understand the mechanisms underlying this spectrum. Further studies are needed to assess if MAThyS may be use as an indicator of the response to treatment.

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Table 1. The hypothesised structure of the MAThyS: description of the five a priori dimensions of the MATHYS (emotion, cognition, psychomotor function, motivation, sensory perception) with the corresponding items.

Postulated Dimensions	EMOTION (EM)	COGNITION (CO)	PSYCHOMOTOR FUNCTION (MO)	MOTIVATION (VO)	SENSORY PERCEPTION (SE)
Items number:	3, 7, 10, 18	5, 9, 12, 14	2, 11, 19	4, 15, 16, 17	1, 6, 8, 13, 20
Continuum	Hypo-reactivity / Hyper-reactivity	Retardation / Acceleration	Retardation / Agitation	Decrease/ Increase	Decrease / Increase

Table 2. Socio-demographic characteristics of the sample

Tableau 2. Résumé des variables descriptives, ensemble des suje

Effectif (%)	Pop. Tot. (N = 196)	Contrôle (N = 44)	Normothy (N = 43)	EDM (N = 30)	EDM+Ma (N = 28)	Maniaque[1] (N = 51)

Age						
Moyenne	38.36	35.41	39.56	38.90	42.43	37.35
(E-T)	(12.75)	(12.93)	(12.90)	(11.89)	(10.20)	(13.87)
Min-Max	14.00-	22.00-	17.00-	20.00-	19.00-	14.00-
	78.00	67.00	78.00	61.00	60.00	65.00
Médiane						
	39.00	30.00	38.00	41.00	44.00	39.00
Sexe						
Homme	61 (31.12)	17 (38.64)	14 (32.56)	7 (23.33)	4 (14.29)	19 (37.25)
Femme	135 (68.88)	27 (61.36)	29 (67.44)	23 (76.67)	24 (85.71)	32 (62.75)
Statut marital						
Célibataire	71 (36.22)	19 (43.18)	18 (41.86)	7 (23.33)	6 (21.43)	21 (41.18)
Marié/concubinage	85 (43.37)	23 (52.27)	18 (41.86)	12 (40.00)	15 (53.57)	17 (33.33)
Séparé/veuf	39 (19.90)	2 (4.55)	7 (16.28)	10 (33.33)	7 (25.00)	13 (25.49)
DM	*1 (0.51)*	*0*	*0*	*1 (3.34)*	*0*	*0*
Groupe du sujet		-	-	-	-	
Contrôle	44 (22.45)					-
Normo	43 (21.94)					-
Hypoman. / Man.	39 (19.90)					39 (76.47)
EDM	30 (15.30)					-
EDM+sympt. man.	28 (14.29)					-
Mixte	12 (6.12)					12 (23.53)
Type de trouble BP		-				
I	92 (60.53)[2]		24 (55.81)	15 (50.00)	8 (28.57)	45 (88.24)
II	60 (39.47)		19 (44.19)	15 (50.00)	20 (71.43)	6 (11.76)

		(N = 196) **%**
Age		
	Mean	38.36 years (±12.75)
Gender		
	Men	61 (31.12)
	Women	135 (68.88)
Marital Status		
	Single	71 (36.22)
	Married/cohabitation	85 (43.37)
	Separated/widowed	39 (19.90)
	Missing value	*1 (0.51)*
Group		
	Control	44 (22.45)
	Normothymic bipolar patients	43 (21.94)
	Hypomanic / Manic episode	39 (19.90)
	Major Depressive episode	30 (15.30)
	Major Depressive episode plus manic symptoms	28 (14.29)
	Mixed	12 (6.12)

Type of bipolar disorders	
Bipolar type I	92 (60.53)[2]
Bipolar type II	60 (39.47)
Suicide attempt during the current episode	
Yes	10 (9.17)[3]
No	99 (90.83)

Table 3. Summary of the descriptive variables for subjects

Controls (N=44)	Emotion	Cognition	Motricity	Motivation	Sensorial	Total Sc.
Mean	21.49	20.61	14.64	20.70	26.14	103.60
(SD)	(2.51)	(2.80)	(2.48)	(3.14)	(2.81)	(9.77)
Median	20.0	20.0	15.0	20.0	25.0	100.5

Normo. (N=43)	Emotion	Cognition	Motricity	Motivation	Sensorial	Total Sc.
Mean	22.96	21.58	14.15	20.62	26.91	106.2
(SD)	(4.46)	(3.94)	(3.31)	(5.52)	(4.32)	(14.50)
Médian	22.5	20.5	15.0	20.0	25.0	102.0

MDE (N=30)	Emotion	Cognition	Motricity	Motivation	Sensorial	Total Sc.
Mean	12.67	11.63	5.05	6.15	18.9	54.42
(SD)	(9.72)	(6.42)	(3.65)	(4.01)	(6.54)	(22.95)
Median	10.8	12.5	3.8	6.0	19.5	54.5

MA (N=44)	Emotion	Cognition	Motricity	Motivation	Sensorial	Total Sc.
Mean	31.49	28.11	18.18	25.93	33.38	137.10
(SD)	(6.61)	(7.15)	(7.62)	(8.97)	(9.68)	(29.95)
Median	33.0	28.3	18.5	26.8	34.3	136.3

Normo.= normothymic bipolar patients , MDE = Major Depressive Episode , MA = Manic and hypomanic Episodes

Table 4 . Item-scale and scale-scale correlations, and internal consistency of hypothesised domains

Total population (N=187)	EM	CO	MO	VO	SE	Total Sc.
Correlation coefficients between items and the scale without the item considered (MTMM).	0.66-0.83	0.41-0.62	0.50-0.63	0.55-0.78	0.44-0.58	0.35-0.69
EMOTIONAL REACTIVITY (EM)	*(0.87)*					
COGNITION SPEED (CO)	0.71	*(0.70)*				
PSYCHOMOTOR function (MO)	0.58	0.64	*(0.75)*			
MOTIVATION (VO)	0.54	0.66	0.70	*(0.84)*		
SENSORY PERCEPTION (SE)	0.57	0.61	0.50	0.63	*(0.74)*	
Correlation coefficients between subscales and the total score without items of the considered Subscale (MTMM).	0.70	0.79	0.72	0.74	0.68	*(0.93)*

Diagonally in italics, Cronbach alpha

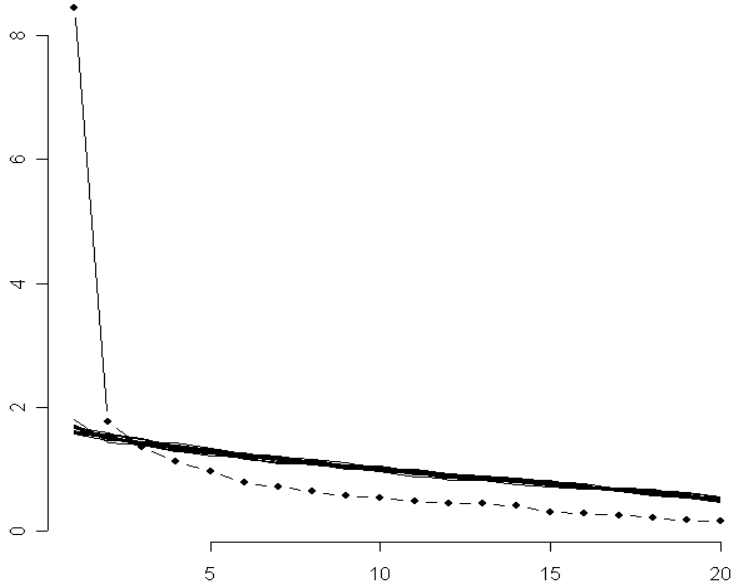**Figure 1. Eigenvalue calculation and diagram, and percentage of variance explained by them (N=187).**

Table 5. MAThyS 2-factor model (Varimax rotation – N=187)

MAThyS VARIMAX (N = 188)	Dimensions	Fact 1 Global fonctionning	Fact 2 Emotional reactivity
	Eigenvalues	42.3	8.8
	% proportion Variable	23.9	22.6
THEO =	% cumulativeVariable	23.9	46.5
SE	1	**0.539**	
MO	2		**0.444**
EM	3		**0.719**
VO	4	**0.542**	
CO	5		
SE	6		
EM	7		**0.809**
SE	8	0.415	**0.539**
CO	9	**0.504**	0.449
EM	10		**0.650**
MO	11	**0.650**	
CO	12		**0.582**
SE	13	**0.465**	
CO	14	**0.498**	
VO	15	**0.845**	
VO	16	**0.836**	
VO	17	**0.582**	
EM	18		**0.877**
MO	19	**0.545**	
SE	20	**0.512**	

Listwise (component <0.4 were removed for most clarity)