





Section V

Appendix

DSM Criteria

DIAGNOSTIC STATISTICAL MANUAL (DSM) CRITERIA FOR THE PSYCHIATRIC DISORDERS STUDIED IN THIS DISSERTATION

ALCOHOL USE DISORDERS

DSM-IV criteria for Alcohol Dependence

A maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance as defined by either of the following:
 - a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
 - b. Markedly diminished effect with continued use of the same amount of alcohol.
2. Withdrawal, as defined by either of the following:
 - a. The characteristic withdrawal syndrome for alcohol.
 - b. Alcohol is taken to relieve or avoid withdrawal symptoms.
3. Alcohol is often taken in larger amounts or over a longer period than was intended.
4. There is a persistent desire or there are unsuccessful efforts to cut down or control alcohol use.
5. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
7. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the alcohol (e.g., continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

DSM 5 proposed revision for Alcohol Use Disorder

(Updated April 30, 2012; consulted online October 2012, at <https://www.dsm5.org>)

A. A problematic pattern of alcohol use leading to clinically significant impairment or distress.

B. Two (or more) of the following occurring within a 12-month period:

1. Alcohol is often taken in larger amounts or over a longer period than was intended
2. There is a persistent desire or unsuccessful effort to cut down or control alcohol use
3. A great deal of time is spent in activities necessary to obtain alcohol, use the substance, or recover from its effects
4. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to alcohol use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
5. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance
6. Important social, occupational, or recreational activities are given up or reduced because of alcohol use

7. Recurrent alcohol use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
8. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
9. Tolerance, as defined by either or both of the following:
 - a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
 - b. Markedly diminished effect with continued use of the same amount of the substance
10. Withdrawal, as manifested by either of the following:
 - a. The characteristic withdrawal syndrome for alcohol (refer to Criteria A and B of the criteria set for Withdrawal)
 - b. The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
11. Craving or a strong desire or urge to use alcohol

Specify the following:

Early Remission. This specifier is used if, for at least 3 months, but for less than 12 months, the individual does not meet any of the criteria 1-10 for a Substance Use Disorder (i.e. none of the criteria except for Criterion 11, "Craving or a strong desire or urge to use a specific substance").

Sustained Remission. This specifier is used if none of the criteria 1-10 for a Substance Use Disorder have been met at any time during a period of 12 months or longer (i.e. none of the criteria met except for Criterion 11, "Craving or a strong desire or urge to use a specific substance").

The following specifier applies as a further specifier of remission (e.g. "early remission in a controlled environment", and "sustained remission in a controlled environment") if the individual is in remission and in a controlled environment:

In a Controlled Environment. This additional specifier is used if the individual is in an environment where access to alcohol and controlled substances is restricted, and no criteria for a Substance Use Disorder have been met. Examples of these environments are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

DEPRESSIVE DISORDER

DSM-IV criteria Major Depressive Episode:

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful).
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day nearly every day (as indicated by either subjective account or observation made by others).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.

4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings or restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

-The symptoms do not meet the criteria for a Mixed Episode.

-The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

-The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

-The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

DSM-IV criteria Major Depressive Disorder:

Single Episode:

1. Presence of a single Major Depressive Episode.
2. The major depressive episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
3. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode.

Recurrent:

1. Presence of two or more major depressive episodes.
2. The major depressive episodes are not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
3. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode.

ANXIETY DISORDERS

DSM-IV criteria Generalized Anxiety Disorder:

1. At least 6 months of "excessive anxiety and worry" about a variety of events and situations. Generally, "excessive" can be interpreted as more than would be expected for a particular situation or event. Most people become anxious over certain things, but the intensity of the anxiety typically corresponds to the situation.
2. There is a significant difficulty in controlling the anxiety and worry. If someone has a very difficult struggle to regain control, relax or cope with the anxiety and worry, then this requirement is met.

3. The presence for most days over the previous six months of 3 or more of the following symptoms:
 - a. Feeling wound-up, tense or restless
 - b. Easily becoming fatigued or worn-out
 - c. Concentration problems
 - d. Irritability
 - e. Significant tension in muscles
 - f. Difficulty with sleep
4. The symptoms are not part of another mental disorder.
5. The symptoms cause "clinically significant distress" or problems functioning in daily life.
6. The condition is not due to a substance or medical issue.

DSM-IV criteria Social Phobia:

1. A persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others.
2. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be embarrassing and humiliating
3. Exposure to the feared situation almost invariably provoked anxiety, which may take the form of a situationally bound or situationally pre-disposed Panic Attack.
4. The person recognizes that this fear is unreasonable or excessive.
5. The feared situations are avoided or else are endured with intense anxiety and distress.
6. The avoidance, anxious anticipation, or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational (academic) functioning, or social activities or relationships, or there is a marked distress about having the phobia.
7. The fear or avoidance is not due to direct physiological effects of a substance or a general medical condition not better accounted for by another mental disorder.

DSM-IV criteria Panic Disorders:

1. Both a and b
 - a. Recurrent unexpected Panic Attacks
 - b. At least one of the attacks has been followed by 1 month (or more) of one (or more) of the following:
 - persistent concern about having additional attacks
 - worry about the implications of the attack or its consequences (e.g., losing control, having a heart attack, "going crazy")
 - a significant change in behavior related to the attacks
2. The Panic Attacks are not due to the direct physiological affects of a substance or a general medical condition.
3. The Panic Attacks are not better accounted for by another mental disorder, such as Social Phobia, Specific Phobia, Obsessive Compulsive Disorder, Posttraumatic Stress Disorder, or Separation Anxiety Disorder.



Abbreviations

AAL	automated anatomical labeling	MDD	major depressive disorder
ACC	anterior cingulate cortex	N	number of participants
AC-PC	anterior commissure – posterior commissure	NEMESIS	Netherlands mental health survey and incidence study
AD	alcohol dependence	NEO-FFI	NEO five-factor inventory
AMC	academic medical center Amsterdam	NESDA	Netherlands study of depression and anxiety
ANOVA	analysis of variance	NIVEL	Nederlands instituut voor onderzoek van de gezondheidszorg
ANCOVA	analysis of covariance	NMDA	N-methyl-D-asparaginezuur
AUDIT	alcohol use disorders identification test	NWO	Dutch organization for scientific research
BA	Brodmann's area	O	outcome
BDNF	brain-derived neurotrophic factor	OFC	orbitofrontal cortex
BAI	Beck anxiety inventory	PET	positron emission tomography
BIS	Barratt impulsiveness scale	PIT	Pavlovian-to-instrumental transfer
BOLD	blood oxygen level dependent	PhD	doctor of philosophy
CI	confidence interval	PHG	parahippocampal gyrus
CIDI	composite international diagnostic interview	PTSD	post-traumatic stress disorder
CIWA-Ar	clinical institute withdrawal assessment	R	response
CRT	cue-reactivity task	RF	radiofrequency
d	effect size	ROI	region of interest
D/A	depression/anxiety	RT	reaction time
DARTEL	diffeomorphic anatomical registration through exponentiated lie algebra	S	stimulus
df	degrees of freedom	SENSE-8	sensitivity encoding for fast MRI (8 coils)
DLPFC	dorsolateral prefrontal cortex	SMA	supplementary motor area
DS	dorsal striatum	sMRI	structural magnetic resonance imaging
DSM	diagnostic manual for the mental disorders	SPM ₅	statistical parametric mapping version 5
DTI	diffusion tensor imaging	SPM ₈	statistical parametric mapping version 8
EPI	echo planar imaging	SPSS	statistical package for the social sciences
EWM	emotional word memory task	SSRI	selective serotonin reuptake inhibitor
FH	family history	SSD	stop-signal delay
FH+	family history positive	SST	stop-signal task
FH-	family history negative	STAI	state-trait anxiety inventory
fMRI	functional magnetic resonance imaging	SS	successful stop-trials
FWE	family wise error rate	SVC	small volume correction
FWHM	full-width at half-maximum	t	student's t-test
GGZ	geestelijke gezondheidszorg	T ₁	structural T ₁ -weighted MRI scan
GLM	general linear model	TE	echo time
GM	gray matter	ToL	tower of London
GO	go-trials	TR	repetition time
HC	healthy control	U	non-parametric Mann-Whitney U-test
IDS	inventory of depressive symptomatology	UMCG	universitair medisch centrum Groningen
LUMC	Leids universitair medisch centrum	VBM	voxel based morphometry
M	mean	VS	ventral striatum
MADRS	Montgomery-Åsberg depression rating scale	VMPFC	ventromedial prefrontal cortex
MNI	Montreal neurologic institute	WHO	world health organization
MPFC	medial prefrontal cortex	WFU	Wake Forest university
MRI	magnetic resonance imaging	X ²	chi-square test

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List of publications

JOURNAL ARTICLES

- De Ruiter, MB, Veltman, DJ, Goudriaan, AE, Oosterlaan, J, **Sjoerds, Z**, van den Brink, W (2009). Response perseveration and ventral prefrontal sensitivity to reward and punishment in male problem gamblers and smokers. *Neuropsychopharmacology* 34 (4): 1027-1038.
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- Sjoerds, Z**, Van den Brink, W, Beekman, ATF, Penninx, BWJH, Veltman, DJ (2013). Response inhibition in alcohol dependent patients and patients with depression/anxiety: an fMRI study. *Psychological Medicine*, Epub ahead of print. DOI: 10.1017/S0033291713002274
- Sjoerds, Z**, De Wit, S, Van den Brink, W, Robbins, TW, Beekman, ATF, Penninx, BWJH, Veltman, DJ. Behavioral and neuroimaging evidence for a bias to the habit system in alcohol dependent patients. *Submitted for publication*.
- Sjoerds, Z**, Van den Brink, W, Beekman, ATF, Penninx, BWJH, Veltman, DJ. Reactivity and craving to alcohol cues in alcohol dependent patients with comorbid depression and anxiety. *Submitted for publication*.
- Luigjes, J, Lorenzetti, V, De Haan, S, Youssef, G, Fontenelle, L, Murawski, C, **Sjoerds, Z**, Van den Brink, W, Denys, D, Yücel, M. What is compulsivity? Towards a definition by disentangling it from habit and impulsivity. *In preparation*.
- Sjoerds, Z**, Luigjes, J, Van den Brink, W, Denys, D, Yücel, M. Habits and drug-use motivations in humans; how do they relate? *In preparation*.
- Sjoerds, Z**, Veltman, DJ, Penninx, BWJH, Van den Brink, W, Stufflebeam, S, Douw, L. Network analysis in alcohol dependence; a progressive disruption in small world properties? *In preparation*.

CONFERENCE PROCEEDINGS

- Sjoerds, Z**, Van den Brink, W, Beekman, ATF, Penninx, BWJH, Veltman, DJ. Response inhibition in alcohol dependent patients: an fMRI comparison with depressed/anxious patients & healthy controls. *68th Annual Meeting of the Society for Biological Psychiatry, San Fransisco (CA), U.S.A.*. 16-18 May 2013 (Nominated for the 2013 Top Poster Award)

- Sjoerds, Z, Van den Brink, W, Beekman, ATF, Penninx, BWJH, Veltman, DJ.** Alcohol cue reactivity is associated with duration & severity of alcohol dependence, not with comorbid depression or anxiety. *Neuroscience Campus Amsterdam Annual Meeting, Amsterdam, The Netherlands.* April 17, 2013.
- Sjoerds, Z, De Wit, S, Van den Brink, W, Robbins, TW, Beekman, ATF, Penninx, BWJH, Veltman, DJ.** The neural basis of reliance on habits in alcohol dependence; goal-directed behavior and habit learning measured by an instrumental learning task during fMRI. *Organization for Human Brain Mapping (OHBM Meeting) 2012, Beijing, China.* 10-14 June 2012.
- Sjoerds, Z, De Wit, S, Van den Brink, W, Robbins, TW, Beekman, ATF, Penninx, BWJH, Veltman, DJ.** The neural basis of reliance on habits in alcohol dependence. *Neuroscience Campus Amsterdam Annual Meeting, Amsterdam, The Netherlands.* April 18, 2012.
- Sjoerds, Z, Van Tol, MJ, Van den Brink, W, Van der Wee, NJA, Aleman, AA, Beekman, ATF, Penninx, BWJH, Veltman, DJ.** Effects of a family history of alcohol dependence on cognitive and emotional functions in patients with mood- and anxiety disorders: an fMRI study. *VU University Medical Center Science Exchange Day.* Amsterdam, The Netherlands. March 9, 2012
- Sjoerds, Z, Van Tol, MJ, Van den Brink, W, Van der Wee, NJA, Aleman, AA, Beekman, ATF, Penninx, BWJH, Veltman, DJ.** The influence of familial alcohol dependence on planning and emotional encoding in affective disorders. *Organization for Human Brain Mapping (OHBM Meeting) 2011, Québec City, Canada.* June 6-10, 2011.
- Sjoerds, Z, Van Tol, MJ, Van den Brink, W, Van der Wee, NJA, Van Buchem, MA, Aleman, AA, Penninx, BWJH, Veltman, DJ.** The influence of familial alcoholism on brain structure: a voxel based morphometry (VBM) study in non-alcoholics with and without family history of alcohol dependence. *FENS Abstr., vol.5, 108.66, 2010. Federation of European Neuroscience Society (FENS) Forum 2010, Amsterdam, The Netherlands.* July 3-7 2010.
- Sjoerds, Z, Van Tol, MJ, Van den Brink, W, Van der Wee, NJA, Van Buchem, MA, Aleman, AA, Penninx, BWJH, Veltman, DJ.** The effects of familial alcoholism on brain volume of non-alcoholics: A VBM study. *Organization for Human Brain Mapping (OHBM Meeting) 2010, Barcelona, Spain.* June 6-10, 2010.
- Sjoerds, Z, Veltman, DJ, Van den Brink, W, De Wit, S, Penninx, BWJH.** The hijacked brain; an fMRI study on the neural correlates of habit formation in alcohol dependence. *Graduate school of neurosciences Amsterdam and Rotterdam (ONWAR) PhD-Retraite, Woudschoten, The Netherlands.* November 19-20, 2009 .

INVITED PRESENTATIONS

- Alcohol dependence (AD) in the brain: from reward to habit driven drug use; a highlight from 4 year neuroimaging research. Chair: Dr. S. Stufflebeam. *Martinos Center for Biomedical Imaging / Harvard Medical School, Boston (MA), U.S.A.* July 2013.
- Alcohol dependence in the brain; a highlight from 4 years neuroimaging research. Chair: Dr. F. Schlagenhauf. *Max Planck Institute of Human and Cognitive Brain Sciences, Leipzig, Germany.* June 2013
- Alcohol dependence in the brain; from reward to habit driven drug use. Chair: Dr. M. Luijten & Prof. Dr. I.H.A. Franken. *Institute of Psychology, Erasmus University, Rotterdam, The Netherlands.* April 2013

- Alcohol dependence in the brain; from reward to habit driven drug use. Chair: Prof. Dr. Z. Demetrovics. *Addiction symposium. Faculty of Psychology, ELTE Univerity, Budapest, Hungary.* February 2013.
- Alcohol dependence accross lifespan and brain; from family history to compulsivity. Chair: Prof. Dr. A. Heinz. *Klinik für Psychiatrie und Psychotherapie der Charité - Universitätsmedizin Berlin, Campus Charité Mitte, Berlin, Germany.* Novemer 2012.
- Alcohol dependence: habits and the brain. Chair: Dr. G. van Wingen, Dr. M. Caan, Prof. Dr. L. Reneman. *Annual symposium of the Brain Imaging Center (le BIC), Academic Medical Center, Amsterdam, The Netherlands.* November 2012.
- The neural basis of habit formation in alcohol dependent patients; an experimental fMRI-study. Chair: Dr. H. Lesscher & Prof. Dr. L. Vanderschuren. *10th Endo- Neuro- Psycho Meeting 2012, Oral Session: New frontiers in alcoholism research. Lunteren, The Netherlands.* May 2012.
- Family history of alcohol dependence: cognitive and emotional functions in mood/anxiety disorders. Chair: Prof. Dr. T.J. de Vries. *Graduate school of neurosciences Amsterdam and Rotterdam (ONWAR) PhD-Retraite, Oral Session: Addiction. Woudschoten, The Netherlands.* November 2011.
- Family history of alcohol dependence: the influence on executive and emotional functions in affective disorders. Chair: Prof. Dr. A.B. Smit. *Neuroscience Campus Amsterdam, Addiction Meeting. Amsterdam, The Netherlands.* May 2011.
- Familial alcoholism and brain structure . Chair: Prof. Dr. G. Fischer. *13th Conference of the European Association of Substance Abuse Research (EASAR). Bad Aussee, Austria.* May 2010.
- The hijacked brain; an fMRI study on the neural correlates of habit formation in alcohol dependence. Chair: Dr. M.J. van Tol & Prof. Dr. D.J. Veltman. *MRI-meeting, VU University Medical Center & Academic Medical Center. Amsterdam, The Netherlands.* November 2009.
- Studying habit formation in alcohol dependence using fMRI: design & methodology. Chair: Dr. J. Cousijn. *Amsterdam Addiction Platform. Amsterdam, The Netherlands.* April 2009.

Curriculum vitae



Zuzsika Sjoerds was born on November 18th, 1982 in Rotterdam, The Netherlands, from a Dutch father, André Sjoerds and a Hungarian mother, Agnes Radványi. As a child she suffered from epilepsy (absences), which she had outgrown before puberty. After years of treatment at the child neurology department of the VU University Medical Center with Dr. Leo Smit she had become interested in the brain.

After finishing gymnasium at the Keizer Karel College in Amstelveen she started studying Psychology at the Faculty of Psychology and Education at the VU University Amsterdam in 2001. Even though her initial ambition was to become a therapist, she soon decided to specialize in brain research by doing a Master in Clinical Neuropsychology of the Adult.

In 2002, she started a job as a research assistant at a study on the effect of light therapy in depressed elderly with Dr. Ritsaert Lieveise and Dr. Marjan Nielen at Stichting GGZ InGeest. Here she was responsible for randomization, instruction and technical support. In 2005 she started to work on an MRI sub-study on the effects of light therapy on the brain and adrenal glands of depressed elderly at the VU University Medical Center.

In 2005 she did a full-time clinical internship at the Department of Medical Psychology, VU University Medical Center. There she performed neuropsychological assessments using a variety of neuropsychological testbatteries. Subsequently, her former internship supervisor Drs. Ted Koene hired her as a test-assistant at her neuropsychological clinic at Medical Center Walborg, Amsterdam.

For her master's thesis she did a research internship at the Academic Medical Center using fMRI to study the neurobiology of pathological gambling, supervised by Dr. Michiel de Ruiter and Prof. Dr. Dick Veltman. Here she learned to perform MRI data analyses with Matlab and SPM. Following her graduation in 2007 she performed MRI analyses as a research assistant on studies by Dr. Kathleen Thomaes and Dr. Eric Ruhé. In 2008 she started her PhD project on the neurobiology of alcohol dependence within a NESDA-satellite study at the VU University Medical Center, supervised by Prof. Dick Veltman and Prof. Wim van den Brink.

As a PhD candidate she was involved in several committees and extra-curricular projects. She helped organizing the PhD-retreats of her graduateschool ONWAR (Graduateschool Neurosciences Amsterdam and Rotterdam) and was a member of the PhD-student board in the visitation committee for the recognition and prolongation of the ONWAR graduateschool. With The Young Academy On Wheels of the KNAW (Royal Dutch Academy of Sciences) she brought science to high schools. In 2010 she helped organize 'Jump the FENS', an official part of the FENS Forum 2010 in the Mekweg Club in Amsterdam. She was also involved in several departmental committees such as the fMRI-instuif committee, organizing biweekly neuroimaging meetings; the Brain Imaging Center committee at the Academic Medical Center; and the party committee of the Psychiatry / Anatomy and Neurosciences departments of the VU University Medical Center.

During her PhD she supervised Bachelor and Master students, and lectured on neuroimaging in addiction during a few courses at the VU University and University of Amsterdam. In February 2013 she visited the addiction department of Prof. Zsolt Demetrovic at the Psychology Faculty, Eötvös Loránd Tudományegyetem University in Budapest, Hungary. There she coordinated and lectured the course 'Neuroimaging in Addiction' to Master and PhD-students.

In the summer of 2013 she was a visiting fellow at the Martinos Center for Biomedical Imaging, Boston, USA, an institute of Harvard Medical School, Massachusetts Institute for Technology and Massachusetts General Hospital. At the lab of Dr. Steven Stufflebeam she performed network analyses on Resting State fMRI data of alcohol dependent patients, together with Dr. Linda Douw.

In October 2013 she defends her PhD Dissertation at the Faculty of Medicine, VU University Amsterdam.

Dissertation Series

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