Internalizing symptoms mediate the relation between acute pain and autism in adults

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Abstract (119/120)

Research on pain in Autism Spectrum Disorder (ASD) is in its infancy, with almost nothing known about how individual differences may predicting pain response in ASD. In the present study, 45 adults (28 male, age 22-48 years) with diagnoses of autism and intellectual delay were observed during vaccination or dental cleaning and their pain behaviours coded and measures of autism symptom severity, anxiety, depression and obsessivity taken. Our findings showed that greater autism severity predicted greater pain response which was partially mediated by anxiety and depression. These data suggest that mental health symptoms are important when considering pain response in autism. Mood must therefore be considered in future research on pain in ASD as well as clinical pain management.

Keywords: Pain, autism, ASD, clinical, Mediation analysis

Introduction

Autism Spectrum Disorder (ASD) is diagnosed based on deficits in social communication and repetitive or restricted behavioural routines (American Psychiatric Association, 2013). Within the domain of repetitive or restricted behavioural routines, sensory abnormalities have been included as a potential diagnostic characteristic, with 'insensitivity to pain or cold' used as the exemplar here. Little objective study however has been conducted on pain response of the individual with ASD or the factors which might predict pain response (Moore, 2015).

Evidence supporting reduced pain response in ASD is found in a range of case studies (Wing, 1976, 1996), as well as in self report from high functioning adults with ASD (Minshew & Hobson, 2008) and parent report (Klintwall et al., 2011; Militerni et al., 2000). However when objective measures of pain, such as observations of potentially painful venepuncture procedures, are made, rather than displaying reduced pain, individuals with ASD appear to show greater behavioural and physiological response, suggesting that pain may be felt more intensely (Nader, Oberlander, Chambers, & Craig, 2004; Rattaz et al., 2013; Tordjman et al., 2009). Further, psychophysically sound experimental pain induction procedures have suggested that individuals with ASD either have the same or lower threshold for pain (Bird et al., 2010; Cascio et al., 2008; Duerden et al., 2015) again suggesting typical or even hyper sensitive pain response.

Greater understanding of factors which underlie any differences in pain response is essential for both the theoretical understanding and the health of this population. Individuals with ASD might be at greater risk of potentially painful episodes, either through co-morbidity with conditions typically associated with pain or painful procedures (Bottos & Chambers, 2006), or through increased likelihood of having accidents requiring medical treatment (Lee, Harrington, Chang, & Connors, 2008). Further, Rattaz et al., (2013) have suggested that in medical situations where pain relief is typically routine, pain relief may only be provided in 50% of cases for children with ASD. This may be of even greater concern in individuals who have moderate-severe intellectual delay (Charman et al., 2011) and the significant percentage of the ASD population with reduced or absent verbal communication (Anderson et al., 2007). Limited research has examined the relationship between IQ and pain in ASD, with one study suggesting that individuals with lower IQ may have higher pain thresholds, suggesting that reduced pain response might be associated with Intellectual Delay (ID). Parents of children with neurological deficits therefore typically need to rely on non-verbal measures of pain behaviour and response, to identify potential pain and distress (Fanurik, Koh, Schmitz, Harrison, & Conrad, 1999; McGrath, Rosmus, Canfield, Campbell, & Hennigar, 1998). These

dificulties may make those individuals with lower cognitive abilities at even greater risk of pain underidentification (Gilbert-MacLeod, Craig, Rocha, & Mathias, 2000; Oberlander, Gilbert, Chambers, O'donnell, & Craig, 1999), therefore supporting the need for more research to test the validity of objective measures of pain behaviour in these populations.

As stated above, the use of proxy measures to identify pain in these individuals is one way to try to understand pain. One promising line of research has been to code facial and bodily behaviours during painful episodes. During episodes of venepuncture, individuals with ASD have shown greater facial activity compared to controls, (Nader et al., 2004) as well as greater self-injurious behaviours immediately following these procedures, suggesting greater pain response. Both of these imply some distress during these treatments (Tordjman et al., 2009). In a final study, Rattaz et al., (2013) examined both facial action codes and coded behaviours on the Non-Communicating Children's Pain Checklist during venepuncture. Here the children with ASD exhibited marginally more pain and non-pain behaviours during venepuncture, however the major finding was that the autism group showed pain behaviours for a longer duration after the pain procedures, compared to the control group. Although the above research suggests some evidence of increased respomse and pain specific behaviour in ASD, this literature is presently limited to venepuncture, as well as the literature observing pain in ASD having been limited to research with children, and therefore nothing is known about how adults with ASD behave whilst in pain.

At present, there is even less information surrounding individual differences in the presentation of pain in ASD. Firstly, we were interested in examining how the severity of symptoms in ASD might relate to pain expression. The relationship between pain expression and autism trait presentation in ASD has been minimally explored so far, with only Coutemanche and Black (2016) having previously examined this link. Here, children with ASD were observed during daily activities, response to pain was coded on the NCCPC-R and scores were correlated with ADOS-2 scores. Children with higher ADOS-2 scores had fewer pain behaviors, suggesting that as autism severity increases, pain reactivity decreases. In addition to the role of autism specific traits, a number of other clinical features have been shown to alter pain response. Others have, however, failed to find evidence of a link between ASD symptomology and psychophysical thresholds (Duerden et al. 2015; Yasuda et al, 2016). In particular, here we are interested in the potential role of co-occurring internalising symptoms, specifically, psychopathological states in ASD (psychosis, depression, anxiety and OCD). Population studies have suggested that major psychiatric disorders might occur in up to 75% of individuals with ASD (Joshi et al., 2013). Within these the most frequently reported are depressive/anxiety related

conditions and obsesitivty (Buck et al., 2014), these symptoms are however not universal in ASD (Moss, Howlin, Savage, Bolton, & Rutter, 2015). These individual differences may be important, as the literature on pain experience in general populations has often supported the idea that pain intensity is predicted by depression (Castillo et al., 2013; Wise, Fishbain, & Holder-Perkins, 2007), anxiety (Bair et al., 2013) and psychotic symptoms (Jochum et al., 2006), however effects with obsessive symptoms are less consistent (Fontenelle et al., 2010). The presentation of these symptoms are however often different in ASD and therefore the effects of these symptoms on pain cannot be assumed and should therefore also be explored further.

To date, the evidence surrounding pain response in ASD is mixed, with observations of pain behaviours in children with ASD suggesting increased facial response in some studies during the stimulus, and others findings changes only after the end of 'pain'. At present there are no studies observing pain behaviour during medical procedures in adults with ASD. In the present study, healthy adults with ASD were filmed while receiving their annual influenza vaccination or during a routine dental hygienist treatment. This allowed pain behaviours to be observed during a range of acute settings, expanding on previous research which has only included observations during venepuncture. In particular, vaccination is frequently reported as painful and is very common, with an estimated 12 billion vaccinations given each year (Miller & Pisani, 1999). A further aim of this study was to examine if internalising symptoms of depression, anxiety and obsessivity mediate the relationship between autism severity and pain behaviour.

The hypotheses in this study were first, that there would be a significant correlation between the number of traits of autism observed (autism severity) and magnitude of pain response, and second that the relationship between autism and pain traits would be mediated by internalizing traits of depression, anxiety, and obsessivity.

Methods

Sample

Forty-five adults (28 men) aged between 22 and 48 years of age (M = 33.49; SD = 6.38) with a clinical diagnosis of autism and intellectual delay (ID) in the mild to borderline range participated in this study. Participants were recruited from two health care facilities that serves people with ASD and ID, and these adults were required to have resided there for at least a year. The facilities consist of individual homes that are under 24-hour supervision. If no consent was obtainable, or if the patient or patient's family refused the study, the patient was not included. Of the 51 potential participants, 3 declined to participate.

These care centers provide medical, educational, nursing, and mental health services. This project is a community-oriented project available to adult citizens with ASD; however, participants for this study were a specific sample of adults who met study inclusion criteria. Participants met the following inclusion criteria: (a) were diagnosed as having ASD by using the ASD-DA questionnaire (Matson, Wilkins, Boisjoli, & Smith, 2008); (b) were either not taking psychiatric medications at initial assessment or were taking a stable dose of psychiatric medications at least two months at the same dosage prior to the initial assessment, and (c) if psychiatric medications were being used, participants maintained the same dosage throughout the study.

Instruments

Non-Communicating Adults Pain Checklist (NCAPC; (Lotan, Moe-Nilssen, Ljunggren, & Strand, 2010)).

The NCAPC is an 18 item scale, and each item is scored 0–3 referring to the frequency of an observed behavior: 0 = not at all, 1 = just a little, 2 = fairly often, and 3 = very often. These behaviors include vocal reaction, emotional reaction, facial reaction, body language, protective reaction and physiological reaction. The total score ranges from 0 (no pain behavior observed) to 54 (maximal frequency of all pain behaviors observed). Scoring was based on pain behaviors observed during a pre-defined, one hour time period. The NCAPC scale has been found to hold high internal consistency in previous studies (alpha = 0.77) (Lotan et al., 2009) and in the present study (alpha = .83) as well as strong interrater reliability (Lotan et al., 2009), suggesting this is easy and reliable to use. Also NCAPC has sensitivity to distinguish between pain and non-pain situations and between different types of pain situations and pain experiences (Lotan *et al*. 2010). In this study the interrater reliability for NCAPC was .81. Two independent observers completed the NCAPC during the procedures, and scores were averaged.

Autism Spectrum Disorders-Diagnosis for Adults (ASD-DA; (Matson, Wilkins, Boisjoli, & Smith, 2008)).

The ASD-DA was used to measure autistic traits, which is the independent variable in this study. The ASD-DA consists of 31-item, informant-based measure used to assess symptoms associated with ASD. The items of the ASD-DA correspond to different behavioural symptom patterns exhibited by adults with ASD and are scored on a two-point scale with ‘‘0’’ for ‘‘not different, no impairment’’ or ‘‘1’’ for ‘‘different, important impairment.’’ Instructions state that the individual being assessed should be compared to others of similar age living in the

community. The measure can be administered and scored in approximately 10 minutes. The measure has good test-retest and interrater reliability, and internal consistency is robust (Cronbach's α = .94; Matson, Wilkins, & Gonzalez, 2007). The diagnostic utility of the ASD-DA has also been demonstrated by the establishment of cut-off scores for differentiating ASD from controls and ASD from PDD-NOS in adults with ID (Matson, Boisjoli, Gonzalez, & Smith, 2008). The cut-off score was 24.68 (Matson et al., 2007). The scale was applied by a clinical psychologist with several years of expertise in adults with autism.

The Psychopathology in Autism Checklist (PAC) (Helverschou, Bakken, & Martinsen, 2009)

The PAC is a screening checklist completed by caregivers designed to identify adults with autism and ID, in need of psychiatric services. The PAC contains 30 items representing symptoms previously evaluated as specific to one of four major psychiatric disorders (psychosis, depression, anxiety and OCD) and not related to autism. All 42 items are based on ICD-10 and DSM-IV criteria. Carers are asked to assign a score from 1 to 4 (1 = no problem; 2 = minor problem; 3 = moderate problem; 4 = severe problem) for each symptom presented. For the purposes of this paper, the total score was calculated across the three subscales of PAC: anxiety (6 items), depression (7 items), and OCD (7 items). The cut-off scores were: anxiety ≥1.8; depression ≥2.0; OCD ≥2.4 (Bakken et al., 2010). The psychometric properties of the PAC were acceptable with Cronbach's Alpha=.78-.89 (Helverschou et al., 2009). The respondents were care staff members. Criteria for being a rater included having known the person for more than one year and having daily social interaction with the person.

Data Collection Procedure

Assessment during dental hygiene treatment: Every participant was observed for a 10 minute period during the dental hygiene treatment. All dental hygiene treatments were performed by the same dental hygienist. This procedure involved the removal of bacterial plaque and calculus from the tooth surface using an ultrasonic scaler. This is a mechanical instrument consisting of an electric generator, hand piece, and scaling tip. The scalers have water flow delivery through the tip itself, or external water flow delivery through a separate tube attached to the tip. High frequency electrical currents are converted into rapid vibrations in the scaling tip, and when placed on the tooth, shatters plaque and calculus from the surface. The procedure can produce acute discomfort and pain, and typically requires light pressures

applied in overlapping strokes on all surfaces and any exposed root of the tooth. The observer was standing on the right hand of the treatment table, with a clear view of the body and face of the participant.

Assessment during injection: Influenza vaccination took place in a medical center within the National System of Health specializing in the medical care of people with ASD. Injection was performed by a specialized nurse using a standard 25 gage hypodermic needle. The participants received the injection seated in a chair opposite the nurse's table. Every participant was observed during the whole length of the injection time (mean 10 seconds).

The responsible ethics commission of the Nuevo Horizonte Association reviewed and approved this study. An explanation of the study was given to participants, and their families before the study was initiated. Informed consent was provided by all participants or their guardians. Participants were recruited from a specialized residential community for individuals with ASD and other institutions for people with Autism, in Spain. All participants were comprehensively assessed by a proxy therapist group (three professionals) who were blind to the research objectives. The caregivers involved in the study were trained to use the rating scales using four videos of people not used in the current analyses, this ensured consistent approach to the observations. As the aim of the current research was to examine general pain behaviors in ASD rather than responses to individual procedures, the behavioural scores were averaged for each participant across their dental cleaning and influenza procedures.

Results

Correlations

Initially the bivariate correlations among pain total score, severity of ASD, indicators of internaziling symptoms (anxiety, depression, and obsessive-compulsive) were examined.

Table 1

Table one shows that there was a significant correlation between autism severity and pain scores suggesting that, contrary to what the bulk of the existing literature would predict, the greater the severity of autism symptoms in patients, the more pain behaviour they exhibited. Further, these data appear to indicate that ASD severity is related to both anxiety and depression but not obsessivity, supporting suggestions of co-occurrence between autism and poorer mental wellbeing (Moss et al., 2015). A further matter of interest here is that pain

severity was also correlated with anxiety and depression, supporting previous research in the general population, however obsessivity was not related to any of the other variables suggesting that this may play a very small, or no role in pain experience in ASD.

Regression analysis

Table 2

Hierarchical multiple regression was performed to investigate the ability of internaziling symptoms (anxiety, depression, and obsessivity) to predict levels of pain intensity, after controlling for autism severity. Preliminary analyses were conducted to ensure no violation of the assumptions of normality, linearity, and homoscedasticity. Using pain intensity as the dependent variable, the ASD-DA variable was entered on step one, to control the influence of severity of autism on pain total score. This model was statistically significant $F(1, 43) = 26.93$; $p < .001$ and explained 39 % of variance in pain intensity. After entry of internaziling symptoms at step 2, the total variance explained by the model as a whole was 56% ($F(4, 40) = 12.68$; $p < .001$). In the final adjusted model, three out of four predictor variables were statistically significant, with ASD-DA recording a higher Beta value ($\beta = .33$, $p < .01$) than anxiety ($\beta = .31$, $p < .01$) and extraversion ($\beta = .30$ $p < .01$)

Mediation analysis

Model 4 of the PROCESS macro was used to determine whether the indirect (mediating) effects of the three internaziling symptom categories (anxiety, depression and obsessivity) on the ASD-DA Pain intensity-relationship are significant (see Figure 1). The multiple mediator model, in which all of the mediational scales were entered simultaneously, allowed investigation of the indirect effects of the different scales. Figure 1 illustrates the association between the proposed independent variable (autistic traits or ASD-DA scores) and the dependent variable (pain total score) through the three mediators (anxiety, depression and obsessivity). We found that anxiety and depression scores mediated or explained the effects of autistic symptoms on intensity of pain. The total model explained 62% of the variation in Intensity of pain ($R = 0.62$; $F = 20.93$, $P < 0.001$). As can be seen in Fig. 1 and Table 2, the total (c path) and direct effects (c' paths) of the ASD-DA total score on the pain total score were 1.66, $p < .001$ (95% CI: 1.02 to 2.31) and .89, $p < .01$ (95% CI: .18 to 1.59) respectively. The difference between the total and direct effects is the total indirect effects through the three mediators with a point estimate of 0.78 and a 95% BCa bootstrap confidence interval of .32 to 1.44. That is, the difference between the total and the direct effect of the ASD-DA total score

(autistics traits) on the pain total score was unequal zero. An analysis of the specific indirect effects indicated that anxiety and depression were mediators as its 95% confidence intervals did not contain zero. However, the obsessivity did not contribute to the indirect effect.

Table 3

Figure 1

Note: a1, a2, a3, = direct effects of independent variable (IV) on mediators (a paths); b1, b2, b3, = direct effects of mediators on DV (b paths); c = total effect of IV on dependent variable (DV) (c path); c' = direct effect of IV on DV (c prime path); * P < 0.05; ** P < 0.01; *** P < 0.001.

Discussion

The purpose of this research was to examine weather autism severity predicted magnitude of pain behaviours and whether this relationship was mediated by anxiety, depression, and obsessivity. Here we observed a significant relationship between autism severity and total pain report, consistent with individuals who had greater autism severity also showing greater pain behaviours. Further mediation analyses were able to identify that the relationship between autism severity and pain response was partially mediated by the mood variables of anxiety and depression. These findings are therefore in support of our hypotheses.

Although we have supported the proposition that there would be a correlation between pain behaviors and ASD symptom severity, the direction of this effect runs contrary to the only previous study to explore this relationship. Here we found that individuals with ASD who have greater symptom presentation also show more pain behaviors, whereas Coutemanche and Black (2016) found that autism severity predicted reduced pain behavior. There are a number of potential explanations for why these opposing findings may have occurred. First, the ages were very different between the populations, here we examined response in adults where Coutemanche and Black examined pain response in children. It is possible that during development, those with less severe presentation of symptoms learn to regulate their response to a wide variety of stimuli which is not present in children and this may explain the differences between these two studies. Further measurement differences may partially explain these differences. In Coutemanche and Black's study, ADOS-2 scores were used to measure autism severity, whereas in the current study the ASD-DA was used. The ADOS 2 is looking at the magnitude of a set of behaviors, whereas the ASD-DA uses a scoring

method of a behavior being simply present or absent. It is clear, given these contradictions, that more work is needed to examine the link between autism severity and pain response.

The current findings also add to the existing literature in ASD which suggests that individual differences factors, such as self-injurious behaviours (Duerden et al., 2014; Duerden et al., 2012) or intellectual function (Duerden et al., 2015), may influence pain response by adding mood variables as a further factor. This is not at all surprising given that the literature in neurotypical populations has frequently found effects of the mood variables of depression (Castillo et al., 2013; Wise et al., 2007) and anxiety (Bair et al., 2013) on pain perception. These data provide clear support for the need to consider individual differences variables when examining pain response in individuals with Autism Spectrum Disorders. These individual differences may help to further explain some of the current contradiction in findings on pain in ASD.

At present, the literature on pain in ASD suggests that pain behaviour observed outside of medical and research environments is reduced, compared to neurotypical populations (Klintwall et al., 2011; Militerni et al., 2000; Minshew & Hobson, 2008; Wing, 1976, 1996). However, when participants are observed during potentially painful venepuncture procedures in a medical setting, rather than reduced pain beahviour, individuals with ASD appear to show greater behavioural and physiological response, suggesting that pain may be felt more intensely (Nader et al., 2004; Rattaz et al., 2013; Tordjman et al., 2009). Further, psychophysically sound investigations suggest that individuals with ASD either have the same or lower threshold for pain (Bird et al., 2010; Cascio et al., 2008; Duerden et al., 2015), again suggesting typical or even hyper-sensitive pain response. It is possible that the focused nature of medical procedures or experimental investigation, result in the individual with autism experiencing greater negative mood effects and therefore this increase in anxiety drives up pain response under these circumstances. When the individual is in their typical environment however, they may feel less negative affect and anxiety and therefore reduced pain response. It is clearly critical for future research to examine these effects in more detail and establish further the role of mood and other individual differences in pain response in ASD. Further, a greater understanding of the social and environmental context of pain experience in ASD is needed to understand this problem.

A further benefit of the current study is to expand the population demographics and measurement tools used to examine pain in ASD. At present, medical observational data on pain in ASD has largely been limited to pediatric populations, here we were able expand this to examine pain behaviors in adults with ASD. This research has provided data using the NCAPC and demonstrated that this is a valuable tool to understanding pain behaviors in adults with

ASD. This builds upon the work of Rattaz et al. (2013) who were able to show that the child counterpart (Non-Communicating Child Pain Checklist) is a successful measure of pain in children with ASD. The similarity in the design of these two measures suggests that future study might be able to examine pain behaviours across a wider developmental time course, pooling data for these two scales.

These data also present clear clinical implications for those engaging in medical care for those with ASD. Research in the general population has established that negative pain expectations (Gavaruzzi et al., 2010) and pain fear (Koenen et al., 2017) predict greater pain intensity. Here techniques to improve relaxation have been shown to reduce experience of pain (Kemani et al., 2015). If these data are found to be replicable and reliable, then during medical procedures it would be essential to manage expectations around the experiences and manage anxiety to hopefully reduce the reported pain. By reducing behaviours associated with pain and distress, one might also expect that it may also be easier to perform these medical procedures on a more sedate patient.

It is however essential to also consider the limitations of this study. First amongst these is that although the current study recruited a reasonably large sample of participants with ASD, we did not have a control group. This means that although we can comment on data suggesting that severity of autism symptoms related to increased pain response, it is not possible to consider if the pain behaviors are similar to, or different to neurotypical behaviors, or if the magnitude of pain response is similar, elevated or decreased. In the future, the addition of a control group would add additional power to this research.

A further limitation here comes from the use of a population who have either limited verbal communication and/or impaired intellectual functioning. Although it is important to examine these effects in this vulnerable subpopulation of those with ASD, this does mean that we are unable to use self-report to validate that the behaviors observed here are a result of a painful response to the needle insertion. It is also possible that these behaviors may be elicited in response to other factors, such as general somatosensory distress or being in an unfamiliar environment. Although there have been recent suggestions in some clinical conditions that observations of pain behaviors may be a more objective and accurate measure of pain experiences (i.e. depression (Lautenbacher, Bär, Eisold, & Kunz, 2016), it is not yet clear if this is the case for ASD. The use of facial expressions and behaviour as signals of internal states, such as pain, may be a particular challenge in ASD, as it is not clear how the social communicative deficits in this population may contribute to altered pain behaviors. A further limitation here, is that we were not able to directly test the role of intellectual functioning on pain response in this study. All participants were drawn from a center specializing in

individuals with a similar level of intellectual functioning, and intellectual level was assessed in order to make a categorical division, rather than to allow for a linear metric of 'IQ'. In future studies, a consideration of both a wider demographic range and the role of intellectual functioning in pain processing would be of great value.

In conclusion, the present study found that for individuals with ASD, that their pain response was greater as the symptom severity increased. Furthermore the relationship between autism severity and pain was mediated by the mood factors of anxiety and depression. These findings expand previous research and provide a potential explanation for the differences between self-report of pain and pain behavior in the real world, which has suggested reduced pain response in ASD, and the procedural pain observations and experimental pain models may be a result of differences in the anxiety provoked during these activities. These findings also suggest that managing negative mood may be important during medical procedures in ASD.

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Table 1. *Bivariate Pearson correlations of the dependent, independent and moderating variables*

	Mean	SD	Range	2	3	4	5
1. Pain Total	15.71	3.20	8-24	.621**	.592**	.572**	.111
2. ASD-Autism	26.27	1.19	24-29		.507**	.452**	.178
3. Anxiety	2.71	.84	1-4			.391**	.214
4. Depression	2.38	1.03	1-4				.016
5. Obsessivity	1.56	.78	1-4				

Table 2. *Hierarchical Regression Model of Pain total score.*

		R2	R2 Change	B	SE	β	T
Step 1 (Enter)		.39***					
	ASD-Autism			1.66	.32	.62	5.19***
Step 2 (Enter)		,56**	.17**				
	ASD-Autism			,88	,35	,33	2,55**
	Anxiety			1,18	,48	,31	2,5**
	Depression			,94	,38	,30	2,49**
	Obsessivity			-,08	,44	-,02	-,18

Table 3 . *Summary of multiple mediator model analysis of autistic traits on Pain total score through internalizing symptoms (anxiety, depression, and obsessivity).*

		Consequent												
		M1 (Anxiety)			M2 (Depression)			M3 (Obsessivity)				Y (Pain Total score)		
Antecedent		Coeff.	SE	*p*	Coeff.	SE	*p*	Coeff.	SE	*p*		Coeff.	SE	*p*
X (ASD-DA)	a_1	,36	,36	.00	a_2 ,39	,12	.00	a_3 ,12	,10	.24	c'	,89	,35	.01
M1 (Anxiety)		—	—	—	—	—	—	—	—	—	b_1	1,18	.48	.02
M2 (Depression)		—	—	—	—	—	—	—	—	—	b_2	.94	.38	.02
M3 (Obsessitivity)		—	—	—	—	—	—	—	—	—	b_3	-.08	.44	.86
Constant	i_{M1}	-6,69	2,44	.01	i_{M2} -7,86	3,08	.01	i_{M3} -1,51	2,59	.56	i_Y	-12.84	8.35	.13
		R^2= .26			R^2= .20			R^2= .03				R^2 = .56		